ATTACHMENT 1

IMS INSTITUTE
FOR
HEALTHCARE INFORMATICS

May 2016

Advancing Academic Research

Bibliography of Published Papers and Presentations Using IMS Health Information

Introduction

IMS Health information is used extensively by researchers around the world to advance understanding of key healthcare issues. As a leading global information and technology services company, we collaborate with academics and others whose research would be significantly advanced through access to IMS Health proprietary information. This activity generates a large number of peer-reviewed publications and conference presentations, covering a broad range of topics.

The range of information accessed and used for research purposes is extensive. It includes summarized global and national prescription drug volume and sales information; provider-level prescription information; de-identified longitudinal patient data; provider profiles and organizational relationships; and commercial insurance medical and pharmacy claims information.

This bibliography provides a summary of research published from January 2010 through March 2015 that was undertaken by U.S.-based researchers and utilized IMS Health data assets. The bibliography is in reverse chronological order by publication date and organized into four themes: Understanding Disease and Treatment Patterns, Providing Content for Healthcare Costs, Assessing Policy Levers, and Advancing Real World Patient-Level Clinical Evidence. Collectively, this research represents a substantial advancement in understanding the real-world operation of our health system, and is invaluable to multiple stakeholders. This bibliography has been produced as a public service without industry or government funding.

Murray Aitken
Executive Director
IMS Institute for Healthcare Informatics

IMS Institute for Healthcare Informatics, 100 IMS Drive, Parsippany, NJ 07054, USA
info@theimsinstitute.org www.theimsinstitute.org

Contents

Understanding Disease and Treatment Patterns

Metformin prescription patterns among US adolescents aged 10-19 years: 2009-2013

J Clin Pharm Ther. 2016 Apr;41(2):229-36

Wang T, McNeill AM, Chen Y, Senderak M, Shankar RR

Prescriptions, nonmedical use, and emergency department visits involving prescription stimulants

J Clin Psychiatry. 2016 Mar;77(3):e297-304

Chen LY, Crum RM, Strain EC, Alexander GC, Kaufmann C, Mojtabai R

Patient, physician and organizational influences on variation in antipsychotic prescribing behavior

J Ment Health Policy Econ. 2016 Mar;19(1):45-59

Tang Y, Chang CC, Lave JR, Gellad WF, Huskamp HA, Donohue JM

Tablet/capsule size variation among the most commonly prescribed medications for children in the USA: retrospective review and firsthand pharmacy audit

Paediatr Drugs. 2016 Feb;18(1):65-73

Jacobsen L, Riley K, Lee B, Bradford K, Jhaveri R

A US claims-based analysis of real-world lipid-lowering treatment patterns in patients with high cardiovascular disease risk or a previous coronary event

Am J Cardiol. 2016 Feb 15;117(4):495-500

Quek RG, Fox KM, Wang L, Li L, Gandra SR, Wong ND

IUD services among primary care practices in New York City

Contraception (2015)

Jacobson L, Garbers S, Helmy H, Roobol H, Kohn J, Kavanaugh M

Epidemiology and treatment of new-onset and established rheumatoid arthritis in an insured US population

Arthritis Care Res (Hoboken). 2015 Dec;67(12):1646-55

Crane MM, Juneja M, Allen J, Kurrasch RH, Chu ME, Quattrocchi E, Manson SC, Chang DJ

National trends in ambulatory oral anticoagulant use

Am J Med. 2015 Dec;128(12):1300-1305

Barnes GD, Lucas E, Alexander GC, Goldberger ZD

One-year treatment persistence with local estrogen therapy in postmenopausal women diagnosed as having vaginal atrophy

Menopause. 2015 Nov;22(11):1197-203

Portman D, Shulman L, Yeaw J, Zeng S, Uzoigwe C, Maamari R, Iyer NN

Lipid-lowering treatment patterns among patients with type 2 diabetes mellitus with high cardiovascular disease risk

BMJ Open Diabetes Res Care. 2015 Sep 23;3(1)

Quek RG, Fox KM, Wang L, Li L, Gandra SR, Wong ND

Association between outpatient antibiotic prescribing practices and community-associated clostridium difficile infection

Open Forum Infect Dis. 2015 Aug 11;2(3)

Dantes R, Mu Y, Hicks LA, Cohen J, Bamberg W, Beldavs ZG, Dumyati G, Farley MM, Holzbauer S, Meek J, Phipps E, Wilson L, Winston LG, McDonald LC, Lessa FC

Prevalence of bone metastases and bone-targeting agent use among solid tumor patients in the United States

Clin Epidemiol. 2015 Jul 17;7:335-45

Hernandez RK, Adhia A, Wade SW, O'Connor E, Arellano J, Francis K, Alvrtsyan H, Million RP, Liede A

Benzodiazepine use in the United States

JAMA Psychiatry. 2015 Feb 1; 72(2):136-42

Olfson M, King M, Schoenbaum M

Impact of abuse-deterrent OxyContin on prescription opioid utilization

Pharmacoepidemiol Drug Saf 2015;24(2): 197-204

Hwang CS, Chang H-Y, Alexander GC

Comparison of the risks of shopping behavior and opioid abuse between tapentadol and oxycodone and association of shopping behavior and opioid abuse

Clin J Pain. 2014 Dec;30(12): 1051-6

Cepeda MS, Fife D, Kihm MA, Mastrogiovanni G, Yuan Y

Use of a claims database to characterize and estimate the incidence rate for Castleman disease

Leuk Lymphoma. 2014 Sep 29:1-9

Munshi N, Mehra M, van de Velde H, Desai A, Potluri R, Vermeulen J

Impact of the ENHANCE trial on the use of ezetimibe in the United States and Canada

American Heart Journal 2014;167(5):683-689

Lu L, Krumholz HM, Tu JV, Ross JS, Ko DT, Jackevicius CA

Trends in antibiotic resistance in coagulase-negative staphylococci in the United States, 1999 to 2012

Antimicrob. Agents Chemother. 2014;58(3):1404-1409

May L, Klein EY, Rothman RE, Laxminarayan R

Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data

Lancet Infect Dis 2014;14(8):742-750

Van Boeckel TP, Gandra S, Ashok A, et al

Reductions in reported deaths following the introduction of extended-release oxycodone (OxyContin) with an abuse-deterrent formulation

Pharmacoepidemiol Drug Saf 2014;23(12): 1238-1246

Sessler NE, Downing JM, Kale H, Chilcoat HD, Baumgartner TF, Coplan PM

Dipeptidyl peptidase-4 inhibitors and sulfonylureas for type 2 diabetes: friend or foe?

J Diabetes Invest 2014;5(5):475-477

Yabe D, Seino Y

Use of prescription antiobesity drugs in the United States

Pharmacotherapy. 2013 Dec;33(12):1299-307. Epub 2013 Sep 9

Hampp C, Kang EM, Borders-Hemphill V

Medication possession ratio: implications of using fixed and variable observation periods in assessing adherence with disease-modifying drugs in patients with multiple sclerosis

Patient Prefer Adherence. 2013 Jun 12;7: 509-16

Kozma CM, Dickson M, Phillips AL, Meletiche DM

Outpatient antibiotic prescribing, 2010

New England Journal of Medicine 2013;368(15):1461-1462

Hicks LA, Taylor TH, Hunkler RJ

Psychopharmacological prescriptions for people with autism spectrum disorder (ASD): a multinational study

Psychopharmacology 2013;231(6):999-1009

Hsia Y, Wong AYS, Murphy DGM, Simonoff E, Buitelaar JK, Wong ICK

Trends in osteoporosis treatment with oral and intravenous bisphosphonates in the United States, 2002–2012

Bone 2013;57(2):423-428

Wysowski DK, Greene P

The geography of antidepressant, antipsychotic, and stimulant utilization in the United States

Health & Place. 2013; 20: 32-8

King M, Essick C

Should benzodiazepines be replaced by antidepressants in the treatment of anxiety disorders? Fact or fiction?

Psychother Psychosom 2013;82:351–352

Rickels K

Technology diffusion in the antipsychotic market: a comparison of France and the USA between 1998 and 2008

Psychiatr Serv 2013;64(7):680-687

Gallini A, Huskamp HA, Donohue JM

Medication use patterns and predictors of nonpersistence and nonadherence with oral 5-aminosalicylic acid therapy in patients with ulcerative colitis

J Manag Care Pharm. 2012 Nov-Dec;18(9): 701-12

Yen L, Wu J, Hodgkins PL, Cohen RD, Nichol MB

Association between unemployment rates and prescription drug utilization in the United States, 2007–2010

BMC Health Services Research 2012;12(1):435

Kozman D, Graziul C, Gibbons R, Alexander GC

Incidence and predictors of venous thromboembolism (VTE) among ambulatory patients with lung cancer

Lung Cancer 2012;78(3):253-258

Connolly GC, Dalal M, Lin J, Khorana AA

Methotrexate: underused and ignored?

Digestive Diseases and Sciences. 2012; 30(3): 112-8

Herfarth HH, Long MD, Isaacs KL

Patterns of therapy switching, augmentation, and discontinuation after initiation of treatment with select medications in patients with osteoarthritis

Clin Ther. 2011 Dec;33(12):1914-31. Epub 2011 Nov 14 Gore M, Sadosky A, Leslie D, Tai KS, Seleznick M

Persistence with non-selective NSAIDs and celecoxib among patients with gastroesophageal reflux disease and osteoarthritis or rheumatoid arthritis

Curr Med Res Opin. 2011 Feb;27(2):295-302. Epub 2010 Dec 9

Cryer B, Luo X, Assaf AR, Sands G, Mardekian J

New drugs and new molecular entities in dermatology

Arch Dermatol 2011;147(5):568-572

Eaglstein WH, Corcoran G

Prescription opioid analgesics rapidly change the human brain

Pain 2011;152(8):1803-1810

Younger JW, Chu LF, D'Arcy N, Trott K, Jastrzab LE, Mackey SC

Estimating effect of antiviral drug use during pandemic (H1N1) 2009 outbreak, United States

Emerging Infectious Diseases 2011;17(9): 1591-1598 Atkins C

Antimicrobial prescription data reveal wide geographic variability in antimicrobial use in the United States, 2009

Infectious Diseases Society of America. Oct 2010

Hicks LA, Suda KJ, Roberts RM, Hunkler R, Taylor TH Jr., Danziger LH

Lack of improvement in outpatient management of congestive heart failure in the United States

Arch Intern Med 2010;170(15):1399-1400

Banerjee D, Stafford RS

Drug therapies for Parkinson's disease: a database analysis of patient compliance and persistence

The American Journal of Geriatric Pharmacotherapy 2010;8(4):374-383

Tarrants ML, Denarié MF, Castelli-Haley J, Millard J, Zhang D

Providing Context for Healthcare Costs

Increasing economic burden of tyrosine kinase inhibitor treatment failure by line of therapy in chronic myeloid leukemia

Curr Med Res Opin. 2016;32(2):289-99

McGarry LJ, Chen YJ, Divino V, Pokras S, Taylor CR, Munakata J, Nieset CC, Huang H, Jabbour E, Malone DC

Variation in rural health information technology adoption and use

Health Affairs (2016): 10-1377

Heisey-Grove DM

Exacerbations, health services utilization, and costs in commercially-insured COPD patients treated with nebulized long-acting β2-agonists

J Med Econ. 2016;19(1):11-20

Chen YJ, Makin C, Bollu VK, Navaie M, Celli BR

Economic burden of HIV antiretroviral therapy adverse events in the United States

Health economics (2015)

Dekoven M, Makin C, Slaff S, Marcus M, Maiese EM

Determinants of US prescription drug utilization using county level data

National Bureau of Economic Research, 2015

Nianogo T, Okunade A, Fofana D, Chen W

The effect of hospital/physician integration on hospital choice

National Bureau of Economic Research, 2015

Baker LC., Bundorf MK, Kessler DP

National trends in prescription drug expenditures and projections for 2015

Am J Health Syst Pharm 2015;72(9):717-736

Schumock GT, Li EC, Suda KJ, et al

Most uninsured adults could schedule primary care appointments before the ACA, but average price was $160

Health Affairs 34, no. 5 (2015): 773-780

Saloner B, Polsky D, Kenney GM, Hempstead K, Rhodes KV

Market power, transactions costs, and the entry of accountable care organizations in health care

Review of Industrial Organization 47, no. 2 (2015): 167-193

Frech III, HE, Whaley C, Handel BR, Bowers L, Simon CJ, Scheffler RM

Economic burden of tyrosine kinase inhibitor treatment failure in chronic myeloid leukemia

Clin Lymphoma Myeloma Leuk. 2015 Nov;15(11)

Knopf KB, Divino V, McGarry LJ, Chen YJ, Pokras S, Munakata J, Taylor C, Ng D, Nieset CC, Huang H

Influenza antiviral expenditures and outpatient prescriptions in the United States, 2003-2012

Pharmacotherapy. 2015 Nov; 35(11):991-7

Suda KJ, Hunkler RJ, Matusiak LM, Schumock GT

The budget impact of orphan drugs in ihe Us and Canada: a 2007-2013 Midas sales data analysis

Value Health. 2015 Nov;18(7):A666

Divino V, DeKoven M, Kim T, Kleinrock M, Wade RL, Kaura S

Clinical and economic burden of breakthrough seizures

Epilepsy. 2015 Oct;51:40-7

Divino V, Petrilla AA, Bollu V, Velez F, Ettinger A, Makin C

Accuracy of annual prescription drug expenditure forecasts in AJHP

Am J Health Syst Pharm. 2015 Oct 1;72(19): 1642-8

Hartke PL, Vermeulen LC, Hoffman JM, Shah ND, Doloresco F, Suda KJ, Li EC, Matusiak LM, Hunkler RJ, Schumock GT

Healthcare costs among patients with excessive sleepiness associated with obstructive sleep apnea, shift work disorder, or narcolepsy

Am Health Drug Benefits. 2014 Sep;7(6): 334-40

Carlton R, Lunacsek O, Regan T, Carroll CA

Treatment patterns and costs for metastatic renal cell carcinoma patients with private insurance in the United States

Clin Genitourin Cancer. 2014 Sep 28. pii: S1558-7673(14)00206-7

Geynisman DM, Hu JC, Liu L, Tina Shih YC

Hidden costs associated with venous thromboembolism: impact of lost productivity on employers and employees

J Occup Environ Med. 2014 Sep;56(9):979-85

Page RL 2nd, Ghushchyan V, Gifford B, Read RA, Raut M, Bookhart BK, Naim AB, Damaraju CV, Nair KV

Comparison of health services use associated with ziprasidone and olanzapine among schizophrenia and bipolar disorder patients in the USA

Clin Drug Investig. 2014 Jul;34(7):491-9

Jiang Y, Ni W, McGinnis JJ

Behind the scenes: sources of complementarity in R&D

Journal of Economics & Management Strategy 2014;23(1):125-148

Ceccagnoli M, Higgins MJ, Palermo V

National health spending in 2012: rate of health spending growth remained low for the fourth consecutive year

Health Aff 2014;33(1):67-77

Martin AB, Hartman M, Whittle L, Catlin A, NHEA Team

National trends in prescription drug expenditures and projections for 2014

Am J Health Syst Pharm 2014;71(6):482-499

Schumock GT, Li EC, Suda KJ, et al

Costs of tumor necrosis factor blockers per treated patient using real-world drug data in a managed care population

J Manag Care Pharm. 2013 Oct;19(8):621-30

Schabert VF, Watson C, Joseph GJ, Iversen P, Burudpakdee C, Harrison DJ

Differences in rates of hypoglycemia and health care costs in patients treated with insulin aspart in pens versus vials

Curr Med Res Opin. 2013 Oct;29(10):1287-96. Epub 2013 Aug 7

Asche CV, Luo W, Aagren M

The economic burden of acute coronary syndromes for employees and their dependents: medical and productivity costs

J Occup Environ Med. 2013 Jul;55(7):761-7

Page RL 2nd, Ghushchyan V, Gifford B, Read RA, Raut M, Crivera C, Naim AB, Damaraju CV, Nair KV

Annual all-cause healthcare costs among influenza patients with and without influenza-related complications: analysis of a United States managed care database

Appl Health Econ Health Policy. 2013 Apr;11(2):119-28

Karve S, Misurski D, Herrera-Taracena G, Davis KL

Perspectives for managed care organizations on the burden of multiple sclerosis and the cost-benefits of disease-modifying therapies

J Manag Care Pharm. 2013 Jan-Feb;19 (1SupplA):S41-53

Owens GM, Olvey EL, Skrepnek GH, Pill MW

Projecting future drug expenditures in U.S. nonfederal hospitals and clinics-2013

Am J Health Syst Pharm 2013;70(6):525-539

Hoffman JM, Li E, Doloresco F, et al

A national evaluation of antibiotic expenditures by healthcare setting in the United States, 2009

J. Antimicrob. Chemother. 2013;68(3):715-718

Suda KJ, Hicks LA, Roberts RM, Hunkler RJ, Danziger LH

The determinants of pricing in pharmaceuticals: Are US prices really so high?

Health Econ 2013;22(11):1377-1397

Cabrales A, Jiménez-Martín S

Prevalence of off-label use and spending in 2010 among patent-protected chemotherapies in a population-based cohort of medical oncologists

J Clin Oncol 2013;31(9):1134-1139

Conti RM, Bernstein AC, Villaflor VM, Schilsky RL, Rosenthal MB, Bach PB

Medical service encounters and payments associated with topical adjunctive therapy use of timolol for glaucoma

Clin Drug Investig. 2012 Dec;32(12):835-42

Schmier JK, Covert DW, Lau EC

Healthcare utilization and comorbidity burden among children and young adults in the United States with systemic lupus erythematosus or inflammatory bowel disease

J Pediatr. 2012 Oct;161(4):662-670.e2. Epub 2012 May 10

Karve S, Candrilli S, Kappelman MD, Tolleson-Rinehart S, Tennis P, Andrews E

Use and costs of prescription medications and alternative treatments in patients with osteoarthritis and chronic low back pain in community-based settings

Pain Pract. 2012 Sep;12(7):550-60
Epub 2012 Feb 5

Gore M, Tai KS, Sadosky A, Leslie D, Stacey BR

Association between oral 5-ASA adherence and health care utilization and costs among patients with active ulcerative colitis

BMC Gastroenterol. 2012 Sep 24;12:132

Mitra D, Hodgkins P, Yen L, Davis KL, Cohen RD

The burden of chronic low back pain: clinical comorbidities, treatment patterns, and health care costs in usual care settings

Spine (Phila Pa 1976). 2012 May 15;37(11): E668-77

Gore M, Sadosky A, Stacey BR, Tai KS, Leslie D

New bundled world: quality of care and readmission in diabetes patients

J Diabetes Sci Technol. 2012 May 1;6(3):563-71

Chen JY, Ma Q, Chen H, Yermilov I

Comparative effectiveness, cost, and utilization of radical prostatectomy among young men within managed care insurance plans

Value Health. 2012 Mar-Apr;15(2):367-75

Shih YC, Ward JF, Pettaway CA, Xu Y, Matin SF, Davis JW, Thompson BP, Elting LS

Impact of the 2008-2009 economic recession on screening colonoscopy utilization among the insured

Clin Gastroenterol Hepatol. 2012 Mar;10(3): 278-84

Dorn SD, Wei D, Farley JF, Shah ND, Shaheen NJ, Sandler RS, Kappelman MD

Cost of self-monitoring of blood glucose in the United States among patients on an insulin regimen for diabetes

J Manag Care Pharm. 2012 Jan-Feb;18(1):21-32

Yeaw J, Lee WC, Aagren M, Christensen T

The burden of chronic low back pain with and without a neuropathic component: a healthcare resource use and cost analysis

J Med Econ. 2012;15(2):245-52. Epub 2011 Dec 5

Mehra M, Hill K, Nicholl D, Schadrack J

Annual costs of tumor necrosis factor inhibitors using real-world data in a commercially insured population in the United States

J Med Econ. 2012;15(2):264-75

Schabert VF, Watson C, Gandra SR, Goodman S, Fox KM, Harrison DJ

Proton pump inhibitors: potential cost reductions by applying prescribing guidelines

BMC Health Services Research 2012;12(1):408

Cahir C, Fahey T, Tilson L, Teljeur C, Bennett K

Growth in US health spending remained slow in 2010; health share of gross domestic product was unchanged from 2009

Health Aff 2012;31(1):208-219

Martin AB, Lassman D, Washington B, Catlin A, NHEA Team

Projecting future drug expenditures--2012

Am J Health Syst Pharm 2012;69(5):405-421

Hoffman JM, Li E, Doloresco F, et al

Clinical comorbidities, treatment patterns, and healthcare costs among patients with fibromyalgia newly prescribed pregabalin or duloxetine in usual care

J Med Econ. 2012;15(1):19-31

Gore M, Tai KS, Chandran A, Zlateva G, Leslie D

Impact of infliximab adherence on Crohn's disease-related healthcare utilization and inpatient costs

Adv Ther. 2011 Aug;28(8):671-83. Epub 2011 Aug 3

Carter CT, Waters HC, Smith DB

Internal versus external R&D: complements or substitutes

Journal of Economic Literature. Aug 2011

Ceccagnoli M, Higgins MJ, Palermo V

Cost of acute hospitalization and post-discharge follow-up care for meningococcal disease in the US

Hum Vaccin. 2011 Jan 1;7(1):96-101. Epub 2011 Jan 1

Davis KL, Misurski D, Miller JM, Bell TJ, Bapat B

Clinical comorbidities, treatment patterns, and direct medical costs of patients with osteoarthritis in usual care: a retrospective claims database analysis

J Med Econ. 2011;14(4):497-507. Epub 2011 Jun 20

Gore M, Tai KS, Sadosky A, Leslie D, Stacey BR

Commercial importation of prescription drugs in the United States: short-run implications

J Health Polit Policy Law 2011;36(2):295-316

Danzon PM, Johnson SJ, Long G, Furukawa MF

Impact of new drugs and biologics on colorectal cancer treatment and costs

American Journal of Managed Care. 2011;17:e160-e168

Karaca-Mandic P, McCullough JS, Siddiqui MA, Van Houten H, Shah ND

Projecting future drug expenditures—2011

Am J Health-Syst Pharm—Vol 68, 2011

Doloresco F, Fominaya C, Schumock GT, Vermeulen LC, Matusiak L, Hunkler RJ, Shah ND, Hoffman JM

Impact of a prior authorization for pregabalin on health plan drug expenditures

Am J Manag Care. 2010 May;16(5 Suppl):S154-9

Bazalo G, Weiss RC, Joshi AV

The discrepancy in attention deficit hyperactivity disorder (ADHD) medications diffusion: 1994-2003--A global pharmaceutical data analysis

Health Policy 2010;97(1):71-78

Lang H-C, Scheffler RM, Hu T-W

A cost-minimization analysis of dexmedetomidine compared with midazolam for long-term sedation in the intensive care unit

Critical Care Medicine 2010;38(2):497-503

Dasta JF, Kane-Gill SL, Pencina M, et al

Trends in home phototherapy adoption in the US: monetary disincentives are only the tip of the iceberg

J Dermatolog Treat 2010;22(1):27-30

Yentzer BA, Feldman SR

Assessing Policy Levers

Effects of regulation and payment policies on nurse practitioners' clinical practices

Medical Care Research and Review (2016)

Barnes, H, Maier CB, Sarik DA, Germack HD, Aiken LH, McHugh MD

Nurse practitioner and physician assistant staffing in the patient-centered medical homes in New York State

Nursing outlook 63, no. 5 (2015): 593-600

Park J

Solo practitioners remain important contributors to primary care

The Journal of the American Board of Family Medicine 28, no. 1 (2015): 7-10

Peikes DN, Dale SB

Electronic medical record adoption in Oklahoma practices: rural-urban differences and the role of broadband availability

The Journal of Rural Health 31, no. 1 (2015): 47-57

Whitacre BE, Williams RS

Patient-centered medical homes and access to services for new primary care patients

Medical Care 53, no. 10 (2015): 857-862

Aysola J, Rhodes KV, Polsky D

The opportunity for medical systems to reduce health disparities among lesbian, gay, bisexual, transgender and intersex patients

Journal of Medical Systems 39, no. 11 (2015): 1-7

Donald C, Ehrenfeld JM

Geographic variation in health IT and health care outcomes: A snapshot before the meaningful use incentive program began

In Healthcare, vol. 3, no. 1, pp. 18-23. Elsevier, 2015

McLaughlin CG, Lammers E

ASHP national survey on informatics: Assessment of the adoption and use of pharmacy informatics in US hospitals—2013

American Journal of Health-System Pharmacy 72, no. 8 (2015): 636-655.

Fox BI, Pedersen CA, Gumpper KF

Appointment availability after increases in Medicaid payments for primary care

New England Journal of Medicine 372, no. 6 (2015): 537-545

Polsky D, Richards M, Basseyn S, Wissoker D, Kenney GM, Zuckerman S, Rhodes KV

Public health departments and accountable care organizations: finding common ground in population health

American Journal of Public Health 105, no. 5 (2015): 840-846

Ingram R, Scutchfield FD, Costich JF

Physician payments under health care reform

Journal of Health Economics 39 (2015): 89-105

Dunn A, Shapiro AH

Primary care appointment availability for new Medicaid patients increased after Medicaid expansion in Michigan

Health Affairs (2015): 10-1377

Tipirneni R, Rhodes KV, Hayward RA, Lichtenstein RL, Reamer EN, Davis MM

Provider perceptions of the electronic health record incentive programs: a survey of eligible professionals who have and have not attested to meaningful use

Journal of General Internal Medicine 30, no. 1 (2015): 123-130

Weeks DL, Keeney BJ, Evans PC, Moore QD, Conrad DA

Physician emergency preparedness: a national poll of physicians

Disaster Medicine and Public Health Preparedness 9, no. 06 (2015): 666-680

SteelFisher GK., Blendon RJ, Brulé AS, Lubell KM, Brown LJ, Batts D, Ben-Porath E

Rural EMR adoption rates overtake those in urban areas

Journal of the American Medical Informatics Association (2015)

Whitacre BE

Oncologists' response to new data regarding the use of epidermal growth factor receptor inhibitors in colorectal cancer

J Oncol Pract. 2014 Sep;10(5):308-14

Dotan E, Li T, Hall MJ, Meropol NJ, Beck JR, Wong YN

Decline in drug overdose deaths after state policy changes — Florida, 2010–2012

Centers for Disease Control and Prevention, Morbidity and Mortality Weekly Report (MMWR). July 4, 2014 / 63(26);569-574

Johnson H, Paulozzi L, Porucznik C, Mack K, Herter B

The effect of regulation and competition on drug supply

The American Society of Health Economists. Jun 2014

Ridley DB, Conti R

Economic benefits of adequate molecular monitoring in patients with chronic myelogenous leukemia

J Med Econ. 2014 Feb;17(2):89-98. Epub 2013 Nov 26

Guérin A, Chen L, Dea K, Wu EQ, Goldberg SL

The budget impact of orphan drugs in the U.S.: A 2007-2013 MIDAS sales data analysis

Blood 2014;124(21):736-736

Divino V, Dekoven M, Wang W, et al

Development times, clinical testing, postmarket follow-up, and safety risks for the new drugs approved by the US Food and Drug Administration: the class of 2008

JAMA Intern Med 2014;174(1):90-95

Moore TJ, Furberg CD

Medical school gift restriction policies and physician prescribing of newly marketed psychotropic medications: difference-in-differences analysis

BMJ 2013;346:f264

King M, Essick C, Bearman P, Ross JS

The effect of Medicare Part D on Parkinson's disease patients: an update (P04.152)

Neurology 2013;80(Meeting Abstracts 1):P04.152

Grubb E, Denarie M, Stuchlak W, McDonald D, Castelli-Haley J

Does exposure to conflict of interest policies in psychiatry residency affect antidepressant prescribing?

Medical Care 2013;51(2):199-203

Epstein AJ, Busch SH, Busch AB, Asch DA, Barry CL

The moral from Sorrell: educate, don't legislate

Health Matrix Clevel 2013;23(1):237-277

Gooch GR, Rohack JJ, Finley M

Effects of FDA advisories on the pharmacologic treatment of ADHD, 2004-2008

Psychiatr Serv 2013;64(4):339-346

Kornfield R, Watson S, Higashi AS, et al

Cost sharing and decreased branded oral anti-diabetic medication adherence among elderly Part D Medicare beneficiaries

J Gen Intern Med 2013;28(7): 876-885

Sacks NC, Burgess JF, Cabral HJ, Pizer SD, McDonnell ME

Delay and restricted access of new molecules in Turkey compared to the United States and European Union

Journal of Market Access & Health Policy 2013;1(0)

Şahin T, Yeşil A, Topcu T

Atomoxetine use during a period of FDA actions

Med Care. 2012 Nov;50(11):987-92

Du DT, Zhou EH, Goldsmith J, Nardinelli C, Hammad TA

State Medicaid programs did not make use of prior authorization to promote safer prescribing after rosiglitazone warning

Health Aff 2012;31(1):188-198

Ross JS, Jackevicius C, Krumholz HM, et al

Antihyperglycemic medication prescribing and state Medicaid program responses to rosiglitazone safety warnings

Health Aff (Millwood) 2012;31(1):188-198

Ross JS, Jackevicius CA, Krumholz HM, et al

Brand loyalty, generic entry and price competition in pharmaceuticals in the quarter century after the 1984 Waxman-Hatch legislation

International Journal of the Economics of Business 2011;18(2):177-201

Berndt ER, Aitken ML

Characterizing markets for biopharmaceutical innovations: Do biologics differ from small molecules? Forum for health economics & policy

Forum for Health Economics & Policy. Jul 2010; 13(1) 1558-9544

Trusheim MR, Aitken ML, Berndt ER

Impact of FDA black box advisory on antipsychotic medication use

Arch. Intern. Med. 2010;170(1):96-103

Dorsey ER, Rabbani A, Gallagher SA, Conti RM, Alexander GC

Off-label use of second-generation antipsychotic agents among elderly nursing home residents

PS 2010;61(2):130-136

Kamble P, Sherer J, Chen H, Aparasu R

Advancing Real World Patient-Level Clinical Evidence

Time on treatment of everolimus and chemotherapy among postmenopausal women with hormone-receptor-positive/human-epidermal-growth-factor-receptor-2-negative metastatic breast cancer: a retrospective claims study in the US

Curr Med Res Opin. 2016;32(2):385-94

Li N, Hao Y, Kageleiry A, Peeples M, Fang A, Koo V, Wu EQ, Guérin A

Using certification to promote uptake of real-world evidence by payers

J Manag Care Spec Pharm. 2016 Mar;22(3):191-6

Segal JB, Kallich JD, Oppenheim ER, Garrison LP Jr, Iqbal SU, Kessler M, Caleb Alexander G

Patterns of treatment switching in Multiple Sclerosis therapies in US patients active on social media: application of social media content analysis to health outcomes research

J Med Internet Res. 2016 Mar 17;18(3)

Risson V, Saini D, Bonzani I, Huisman A, Olson M

Multiple sclerosis prevalence in the United States commercially insured population

Neurology. 2016 Mar 15;86(11):1014-21

Dilokthornsakul P, Valuck RJ, Nair KV, Corboy JR, Allen RR, Campbell JD

Prevalence of Eosinophilic Gastritis, Gastroenteritis, and Colitis: estimates from a national administrative database

J Pediatr Gastroenterol Nutr. 2016 Jan;62(1): 36-42

Jensen ET, Martin CF, Kappelman MD, Dellon ES

Clinical and economic burden associated with cardiovascular events among patients with hyperlipidemia: a retrospective cohort study

BMC Cardiovasc Disord. 2016 Jan 14;16:13

Fox KM, Wang L, Gandra SR, Quek RG, Li L, Baser O

Determinants of saxagliptin use among patients with type 2 diabetes mellitus treated with oral anti-diabetic drugs

BMC Pharmacol Toxicol. 2015 Apr 2;16:8

Saine ME, Carbonari DM, Newcomb CW, Nezamzadeh MS, Haynes K, Roy JA, Cardillo S, Hennessy S, Holick CN, Esposito DB, Gallagher AM, Bhullar H, Strom BL, Lo Re V 3rd

Trends in opioid analgesic–prescribing rates by specialty, U.S., 2007–2012

Am J Prev Med. 2015 Apr

Levy B, Paulozzi L, Mack KA, Jones CM

US outpatient antibiotic prescribing variation according to geography, patient population, and provider specialty in 2011

Clin. Infect. Dis. 2015;60(9):1308-1316

Hicks LA, Bartoces MG, Roberts RM, et al

The heterogeneity of concentrated prescribing behavior: theory and evidence from antipsychotics

Journal of Health Economics 2015;40:26-39

Berndt ER, Gibbons RS, Kolotilin A, Taub AL

Influence of provider and urgent care density across different socioeconomic strata on outpatient antibiotic prescribing in the USA

J. Antimicrob. Chemother. 2015:dku563

Klein EY, Makowsky M, Orlando M, Hatna E, Braykov NP, Laxminarayan R

National trends in the ambulatory treatment of hypertension in the United States, 1997-2012

PLoS ONE 2015;10(3):e0119292

Zhou M, Daubresse M, Stafford RS, Alexander GC

Effect of direct-to-consumer advertising on asthma medication sales and healthcare utilization

Am. J. Respir. Crit. Care Med. 2015

Daubresse M, Hutfless S, Kim Y, et al

Statin use and risk for cataract: a nested case-control study of 2 populations in Canada and the United States

Can J Cardiol. 2014 Dec;30(12):1613-9

Wise SJ, Nathoo NA, Etminan M, Mikelberg FS, Mancini GB

Profile of the average organ non-donor: Can it be used predictively?

P R Health Sci J. 2014 Sep;33(3):129-31

Torres EA, Martínez NA, Martínez P, Ayala AM, Millián D, Rivera C, Saadé M, Davis J

Anticoagulant use for the prevention of stroke in patients with atrial fibrillation: Findings from a multi-payer analysis

BMC Health Serv Res. 2014 Jul 28; 14:329

Lang K, Bozkaya D, Patel AA, Macomson B, Nelson W, Owens G, Mody S, Schein J, Menzin J

Vital Signs: variation among states in prescribing of opioid pain relievers and benzodiazepines — United States, 2012 centers for disease control and prevention, morbidity and mortality weekly report (MMWR)

July 4, 2014 / 63(26);563-568

Paulozzim LJ, Mack KA, Hockenberry JM

Antidepressant dose, age, and the risk of deliberate self-harm

JAMA Intern Med. 2014 Jun;174(6):899-909

Miller M, Swanson SA, Azrael D, Pate V, Stürmer T

Treatment patterns following discontinuation of adalimumab, etanercept, and infliximab in a US managed care sample

Adv Ther. 2014 Apr;31(4):410-25

Yeaw J, Watson C, Fox KM, Schabert VF, Goodman S, Gandra SR

Prescription opioid and heroin abuse

National Institute of Drug Abuse; Apr 2014

Volkow ND

Top 100 selling drugs of 2013

Medscape Medical News. 2014 Jan

Brooks M

Anti-diabetic drug utilization of pregnant diabetic women in us managed care

BMC Pregnancy Childbirth. 2014 Jan 17;14:28

Knox CA, Delaney JA, Winterstein AG

Adherence to statins in primary prevention: yearly adherence changes and outcomes

J Manag Care Pharm. 2014 Jan;20(1):51-7

Slejko JF, Ho M, Anderson HD, Nair KV, Sullivan PW, Campbell JD

Risk of arrhythmias associated with ipratropium bromide in children, adolescents, and young adults with asthma: A nested case-control study

Pharmacotherapy. 2014;34(4):315-23. Epub 2013 Aug 5

Adimadhyam S, Schumock GT, Walton S, Joo M, McKell J, Lee TA

Changes in physician antipsychotic prescribing preferences, 2002–2007

Psychiatr Serv 2014;65(3):315-322

Donohue J, O'Malley AJ, Horvitz-Lennon M, Taub AL, Berndt E, Huskamp H

Trends and seasonal variation in outpatient antibiotic prescription rates in the United States, 2006 to 2010

Antimicrob. Agents Chemother. 2014;58(5):2763-2766

Suda KJ, Hicks LA, Roberts RM, Hunkler RJ, Taylor TH

Emergency hospitalizations for unsupervised prescription medication ingestions by young children

Pediatrics 2014;134(4):e1009-1016

Lovegrove MC, Mathew J, Hampp C, Governale L, Wysowski DK, Budnitz DS

ASHP national survey of pharmacy practice in hospital settings: prescribing and transcribing-2013

Am J Health Syst Pharm 2014;71(11):924-942

Pedersen CA, Schneider PJ, Scheckelhoff DJ

The effect of competing direct-to-consumer advertising campaigns on the use of drugs for benign prostatic hyperplasia: time series analysis

J Gen Intern Med 2014;30(4):514-520

Skeldon SC, Kozhimannil KB, Majumdar SR, Law MR

Geographic and temporal variations in community antibiotic use, Florida, 2010-2012

APHA; 2014

Azarian T

Characterizing the relationship between free drug samples and prescription patterns for acne vulgaris and rosacea

JAMA Dermatol 2014;150(5):487-493

Hurley MP, Stafford RS, Lane AT

Trends in the use of buprenorphine by office-based physicians in the United States, 2003-2013

Am J Addict 2014

Turner L, Kruszewski SP, Alexander GC

Ambulatory treatment of type 2 diabetes in the U.S., 1997-2012

Diabetes Care 2014;37(4):985-992

Turner LW, Nartey D, Stafford RS, Singh S, Alexander GC

Trends of postmenopausal estrogen plus progestin prevalence in the United States between 1970 and 2010

Obstet Gynecol 2014;124(4): 727-733

Jewett PI, Gangnon RE, Trentham-Dietz A, Sprague BL

Male breast cancer and 5α-reductase inhibitors finasteride and dutasteride

J Urol. 2013 Nov;190(5):1811-4. Epub 2013 May 9

Bird ST, Brophy JM, Hartzema AG, Delaney JA, Etminan M

Tamsulosin treatment for benign prostatic hyperplasia and risk of severe hypotension in men aged 40-85 years in the United States: risk window analyses using between and within patient methodology

BMJ. 2013 Nov 5;347:f6320

Bird ST, Delaney JA, Brophy JM, Etminan M, Skeldon SC, Hartzema AG

Long-term patterns of use and treatment failure with anticholinergic agents for overactive bladder

Clin Ther. 2013 Nov;35(11): 1744-51

Chancellor MB, Migliaccio-Walle K, Bramley TJ, Chaudhari SL, Corbell C, Globe D

Rates and predictors of antipsychotic non-adherence and hospitalization in Medicaid and commercially-insured patients with schizophrenia

J Med Econ. 2013 Aug;16(8):997-1006. Epub 2013 Jun 28

Lang K, Federico V, Muser E, Menzin J, Menzin J

Risk of acute kidney injury associated with the use of fluoroquinolones

CMAJ. 2013 Jul 9;185(10):E475-82. Epub 2013 Jun 3

Bird ST, Etminan M, Brophy JM, Hartzema AG, Delaney JA

Current and future disease progression of the chronic HCV population in the United States

PLoS One. 2013 May 21;8(5):e63959. Print 2013

Zalesak M, Francis K, Gedeon A, Gillis J, Hvidsten K, Kidder P, Li H, Martyn D, Orne L, Smith A, Kwong A

Increased risk of pneumocystis jiroveci pneumonia among patients with inflammatory bowel disease

Inflamm Bowel Dis. 2013 Apr;19(5):1018-24

Long MD, Farraye FA, Okafor PN, Martin C, Sandler RS, Kappelman MD

Increased risk of pneumonia among patients with inflammatory bowel disease

Am J Gastroenterol. 2013 Feb;108(2):240-8. Epub 2013 Jan 8

Long MD, Martin C, Sandler RS, Kappelman MD

Increased risk of herpes zoster among 108 604 patients with inflammatory bowel disease

Aliment Pharmacol Ther. 2013 Feb;37(4):420-9. Epub 2012 Dec 13

Long MD, Martin C, Sandler RS, Kappelman MD

Risk of venous thromboembolism in women with polycystic ovary syndrome: A population-based matched cohort analysis

CMAJ. 2013 Feb 5;185(2):E115-20. Epub 2012 Dec 3

Bird ST, Hartzema AG, Brophy JM, Etminan M, Delaney JA

US-based emergency department visits for fluoroquinolone-associated hypersensitivity reactions

Pharmacoepidemiol Drug Saf 2013;22(10): 1099-1106

Jones SC, Budnitz DS, Sorbello A, Mehta H

Analysis of benzonatate overdoses among adults and children from 1969-2010 by the United States Food and Drug Administration

Pharmacotherapy 2013;33(1):38-43

McLawhorn MW, Goulding MR, Gill RK, Michele TM

Impact of oncology-related direct-to-consumer advertising

Cancer 2013;119(5):1065-1072

Abel GA, Chen K, Taback N, Hassett MJ, Schrag D, Weeks JC

Concomitant use of isotretinoin and contraceptives before and after iPledge in the United States

Pharmacoepidemiol Drug Saf 2013;22(12): 1251-1257

Pinheiro SP, Kang EM, Kim CY, Governale LA, Zhou EH, Hammad TA

Recent trends in brand-name and generic drug competition

Journal of Medical Economics 2013;17(3): 207-214

Grabowski H, Long G, Mortimer R

Diffusion of antipsychotics in the US and French markets, 1998-2008

Psychiatr Serv 2013;64(7): 680-687

Gallini A, Donohue JM, Huskamp HA

How quickly do physicians adopt new drugs? The case of second-generation antipsychotics

Psychiatr Serv 2013;64(4): 324-330

Huskamp HA, O'Malley AJ, Horvitz-Lennon M, Taub AL, Berndt ER, Donohue JM

Optimizing antimicrobial prescribing: Are clinicians following national trends in methicillin-resistant staphylococcus aureus (MRSA) infections rather than local data when treating MRSA wound infections

Antimicrob Resist Infect Control 2013;2(1):28

Schweizer ML, Perencevich EN, Eber MR, et al

Independent practice associations and physician-hospital organizations can improve care management for smaller practices

Health Aff (Millwood) 2013;32(8):1376-1382

Casalino LP, Wu FM, Ryan AM, et al

When does adoption of health information technology by physician practices lead to use by physicians within the practice?

Journal of the American Medical Informatics Association 2013;20(e1):e26-e32

McClellan SR, Casalino LP, Shortell SM, Rittenhouse DR

Small physician practices in New York needed sustained help to realize gains in quality from use of electronic health records

Health Aff (Millwood) 2013;32(1):53-62

Ryan AM, Bishop TF, Shih S, Casalino LP

Promotion of prescription drugs to consumers and providers, 2001–2010

PLoS ONE 2013;8(3):e55504

Kornfield R, Donohue J, Berndt ER, Alexander GC

Use of niacin in the United States and Canada

JAMA Intern Med 2013;173(14):1379-1381

Jackevicius CA, Tu JV, Ko DT, de Leon N, Krumholz HM

Surveillance of diversion and nonmedical use of extended-release prescription amphetamine and oral methylphenidate in the United States

Journal of Addictive Diseases 2013;32(1):26-38

Sembower MA, Ertischek MD, Buchholtz C, Dasgupta N, Schnoll SH

Prescription-acquired acetaminophen use and the risk of asthma in adults: a case-control study

Ann Pharmacother. 2012 Dec;46(12):1598-608. Epub 2012 Nov 20

Kelkar M, Cleves MA, Foster HR, Hogan WR, James LP, Martin BC

Comparative multidatabase analysis of dosing patterns and infusion intervals for the first 12 infliximab infusions in patients with rheumatoid arthritis

Clin Ther. 2012 Dec;34(12):2286-92. Epub 2012 Nov 13

Bolge SC, Carter CT, Mueller CS, Bailey RA, Ingham MP

Comparative risk of cerebrovascular adverse events in community-dwelling older adults using risperidone, olanzapine and quetiapine: a multiple propensity score-adjusted retrospective cohort study

Drugs Aging. 2012 Oct;29(10):807-17

Chatterjee S, Chen H, Johnson ML, Aparasu RR

Effect of the clopidogrel-proton pump inhibitor drug interaction on adverse cardiovascular events in patients with acute coronary syndrome

Pharmacotherapy. 2012 Sep;32(9):809-18. Epub 2012 Jun 28

Bhurke SM, Martin BC, Li C, Franks AM, Bursac Z, Said Q

Safety assessment of an anti-obesity drug (sibutramine): a retrospective cohort study

Drug Saf. 2012 Aug 1;35(8):629-44

Tyczynski JE, Oleske DM, Klingman D, Ferrufino CP, Lee WC

Risk of melanoma and nonmelanoma skin cancer among patients with inflammatory bowel disease

Gastroenterology. 2012 Aug;143(2):390-399.e1. Epub 2012 May 11

Long MD, Martin CF, Pipkin CA, Herfarth HH, Sandler RS, Kappelman MD

Impact of 5-HT3 receptor antagonists on chemotherapy-induced nausea and vomiting: a retrospective cohort study

BMC Health Serv Res. 2012 Jul 23;12:215

Lin SJ, Hatoum HT, Buchner D, Cox D, Balu S

Can access limits on sales representatives to physicians affect clinical prescription decisions? A study of recent events with diabetes and lipid drugs

J Clin Hypertens (Greenwich). 2012 Jul;14(7):435-46

Chressanthis GA, Khedkar P, Jain N, Poddar P, Seiders MG

The relationship between use of antidepressants and resource utilization among patients with manic or mixed bipolar disorder episodes: findings from a managed care setting

J Affect Disord. 2012 May;138(3):425-32. Epub 2012 Feb 11

Sussman M, Friedman M, Korn JR, Hassan M, Kim J, Menzin J

Risk of falls and fractures in older adults using atypical antipsychotic agents: A propensity score-adjusted, retrospective cohort study

Am J Geriatr Pharmacother. 2012 Apr;10(2):83-94. Epub 2012 Feb 10

Chatterjee S, Chen H, Johnson ML, Aparasu RR

Assessing opioid shopping behaviour: a large cohort study from a medication dispensing database in the US

Drug Saf. 2012 Apr 1;35(4):325-34

Cepeda MS, Fife D, Chow W, Mastrogiovanni G, Henderson SC

Prescription-acquired acetaminophen use and potential overuse patterns: 2001-2008

Pharmacoepidemiol Drug Saf. 2012 Feb;21(2):226-30. Epub 2011 Sep 13

Gokhale M, Martin BC

Rates of 5 common antidepressant side effects among new adult and adolescent cases of depression: a retrospective US claims study

Clin Ther. 2012 Jan;34(1):113-23

Anderson HD, Pace WD, Libby AM, West DR, Valuck RJ

Clinical characteristics, pharmacotherapy, and healthcare resource use among patients with fibromyalgia newly prescribed pregabalin or tricyclic antidepressants

J Med Econ. 2012;15(1):32-44

Gore M, Tai KS, Chandran A, Zlateva G, Leslie D

Adherence to antiretroviral treatment and correlation with risk of hospitalization among commercially insured HIV patients in the United States

PLoS One. 2012;7(2):e31591. Epub 2012 Feb 24

Sax PE, Meyers JL, Mugavero M, Davis KL

Acute and chronic acetaminophen use and renal disease: a case-control study using pharmacy and medical claims

J Manag Care Pharm. 2012 Apr;18(3):234-46

Kelkar M, Cleves MA, Foster HR, Hogan WR, James LP, Martin BC

Effect of a continuous measure of adherence with infliximab maintenance treatment on inpatient outcomes in Crohn's disease

Patient Prefer Adherence. 2012;6:417-26. Epub 2012 Jun 5

Carter CT, Waters HC, Smith DB

Trends in use of second-generation antipsychotics for treatment of bipolar disorder in the United States, 1998-2009

Psychiatr Serv 2012;63(1):83-86

Pillarella J, Higashi A, Alexander GC, Conti R

U.S. utilization patterns of influenza antiviral medications during the 2009 H1N1 influenza pandemic

Influenza and Other Respiratory Viruses 2012;6(6):e129-e133

Borders-Hemphill V, Mosholder A

The association between leukotriene-modifying agents and spontaneously reported suicide

Drug Information Journal 2012;46(1):99-106

Schumock GT, Gibbons RD, Lee TA, Joo MJ, Stayner LT, Valuck RJ

Seasonality and temporal correlation between community antibiotic use and resistance in the United States

Clin Infect Dis. 2012;55(5): 687-694

Sun L, Klein EY, Laxminarayan R

Changing paradigms in the long-term care market

Intl J of Pharm & Health Mrkt 2012;6(3):267-278

Wozniak L, Hassan M, Benner D

Risk of suicide attempt in asthmatic children and young adults prescribed leukotriene-modifying agents: a nested case control study

J Allergy Clin Immunol. 2012;130:368-75

Schumock GT, Stayner LT, Valuck RJ, Joo MJ, Gibbons RD, Lee TA

Association between the commercial characteristics of psychotropic drugs and their off-label use

Medical Care 2012;50(11):940-947

Graziul C, Gibbons R, Alexander GC

Potential impact of benzodiazepine use on the rate of hip fractures in five large European countries and the United States

Calcif. Tissue Int. 2012;91(1):24-31

Khong TP, de Vries F, Goldenberg JSB, et al

Trends in attention deficit hyperactivity disorder ambulatory diagnosis and medical treatment in the United States, 2000-2010

Acad Pediatr 2012;12(2):110-116

Garfield CF, Dorsey ER, Zhu S, et al

National trends in oral anticoagulant use in the United States, 2007 to 2011

Circ Cardiovasc Qual Outcomes 2012;5(5):

615-621

Kirley K, Qato DM, Kornfield R, Stafford RS, Alexander GC

Trends in neutropenia-related inpatient events

J Oncol Pract 2012;8(3):149-155

Kozma CM, Dickson M, Chia V, Legg J, Barron R

The association between drospirenone and hyperkalemia: a comparative-safety study

BMC Clin Pharmacol. 2011 Dec 30;11:23

Bird ST, Pepe SR, Etminan M, Liu X, Brophy JM, Delaney JA

Clinical characteristics, pharmacotherapy, and healthcare resource use among patients with diabetic neuropathy newly prescribed pregabalin or gabapentin

Pain Pract. 2011 Nov-Dec;11(6):528-39. Epub 2011 Mar 16

Gore M, Tai KS, Zlateva G, Bala Chandran A, Leslie D

Reasons for patient visit to a rural general practitioner (GP) practice in Kwa-Zulu Natal, South Africa compared with those in first world countries

International Journal of Medicine and Medical Sciences. Oct 2011; 3(11): 337-342

Govender II, Mabuza LH, et al

Impact of 5-HT(3) RA selection within triple antiemetic regimens on uncontrolled highly emetogenic chemotherapy-induced nausea/vomiting

Expert Rev Pharmacoecon Outcomes Res. 2011 Aug;11(4):481-8. Epub 2011 Jun 28

Schwartzberg L, Jackson J, Jain G, Balu S, Buchner D

Treatment of tobacco dependence

American Medical Association. Release Date: June, 2011

Steinberg M, Evans RM, Hughes JR, Leone FT, Lipsky M

Risk of new-onset diabetes mellitus associated with beta-blocker treatment for hypertension

Curr Med Res Opin. 2011 Apr;27(4):799-807. Epub 2011 Feb 10

Fonseca V, Sharma PP, Shah M, Deedwania P

Risk of serious cardiac events in older adults using antipsychotic agents

Am J Geriatr Pharmacother. 2011 Apr;9(2): 120-32

Mehta S, Chen H, Johnson M, Aparasu RR

Risk of cardiovascular disease events in patients with type 2 diabetes prescribed the glucagon-like peptide 1 (GLP-1) receptor agonist exenatide twice daily or other glucose-lowering therapies: A retrospective analysis of the LifeLink database

Diabetes Care. 2011 Jan;34(1):90-5

Best JH, Hoogwerf BJ, Herman WH, Pelletier EM, Smith DB, Wenten M, Hussein MA

Outpatient antibiotic prescribing and nonsusceptible Streptococcus pneumoniae in the United States, 1996-2003

Clin. Infect. Dis. 2011;53(7): 631-639

Hicks LA, Chien Y-W, Taylor TH, Haber M, Klugman KP, Active Bacterial Core Surveillance (ABCs) Team

Relationship between leukotriene-modifying agent prescriptions dispensed and rate of suicide deaths by county in the US

Drug Health Patient Saf 2011;3:47-52

Schumock GT, Gibbons RD, Lee TA, Joo MJ, Valuck RJ, Stayner LT

Suicide and prescription rates of intranasal corticosteroids and nonsedating antihistamines for allergic rhinitis: an ecological study

J Clin Psychiatry 2011;72(10):1423-1428

Woo J-M, Gibbons RD, Qin P, et al

Generic-to-branded drug switchback patterns: exploratory analysis and insights from the statin class

J of Pharm Health Serv Rsrch. 2011; 2:217-226

Chressanthis GA, Khedkar P, Jain N, Poddar P, Seiders MG

National trends in ambulatory asthma treatment, 1997–2009

J Gen Intern Med 2011;26(12):1465-1470

Higashi A, Zhu S, Stafford RS, Alexander GC

Trends in menopausal hormone therapy use of US office-based physicians, 2000-2009

Menopause 2011;18(4):385-392

Tsai SA, Stefanick ML, Stafford RS

Use of fibrates in the United States and Canada

JAMA 2011;305(12):1217-1224

Jackevicius CA, Tu JV, Ross JS, Ko DT, Carreon D, Krumholz HM

Trends in US hospitalization rates and rhythm control therapies following publication of the AFFIRM and RACE trials

Journal of Cardiovascular Electrophysiology 2011;22(5):548-553

Martin-Doyle W, Essebag V, Zimetbaum P, Reynolds MR

The diversity of concentrated prescribing behavior: an application to antipsychotics

National Bureau of Economic Research; 2011

Taub AAL, Kolotilin A, Gibbons RS, Berndt ER

An analysis of the root causes for opioid-related overdose deaths in the United States

Pain Medicine 2011;12:S26-S35

Webster LR, Cochella S, Dasgupta N, et al

Antiviral prescribing by office-based physicians during the 2009 H1N1 pandemic

Ann Intern Med 2011;154(1):74-76

Hersh AL, Stafford RS

Small and medium-size physician practices use few patient-centered medical home processes

Health Aff 2011;30(8):1575-1584

Rittenhouse DR, Casalino LP, Shortell SM, et al

Prevalence and global health implications of social media in direct-to-consumer drug advertising

J Med Internet Res 2011;13(3)

Liang BA, Mackey TK

Increasing off-label use of antipsychotic medications in the United States, 1995–2008

Pharmacoepidem. Drug Safe. 2011;20(2): 177-184

Alexander GC, Gallagher SA, Mascola A, Moloney RM, Stafford RS

Relationship of pharmaceutical promotion to antidepressant switching and adherence: a retrospective cohort study

Psychiatr Serv. 2010 Dec;61(12):1232-8

Hansen RA, Chen S, Gaynes BN, Maciejewski ML

Risk of falls and fractures in older adults using antipsychotic agents: a propensity-matched retrospective cohort study

Drugs Aging. 2010 Oct 1;27(10):815-29

Mehta S, Chen H, Johnson ML, Aparasu RR

Association between adherence to calcium-channel blocker and statin medications and likelihood of cardiovascular events among US managed care enrollees

BMC Cardiovasc Disord. 2010 Jun 17;10:29

Chapman RH, Yeaw J, Roberts CS

Risk of cerebrovascular adverse events in older adults using antipsychotic agents: a propensity-matched retrospective cohort study

J Clin Psychiatry. 2010 Jun;71(6):689-98

Mehta S, Johnson ML, Chen H, Aparasu RR

History of "abuse-deterrent" combination opioids

Clinical Reviewer Division of Anesthesia and Analgesia Products CDER/FDA/DHHS; Apr 2010

Pucino F

Changes in glitazone use among office-based physicians in the U.S., 2003-2009

Diabetes Care 2010;33(4):823-825

Cohen A, Rabbani A, Shah N, Alexander GC

Correlating pharmaceutical data with a national health survey as a proxy for estimating rural population health

Population Health Metrics 2010;8(1):25

Cossman RE, Cossman JS, James WL, et al

Responding to an FDA warning — geographic variation in the use of rosiglitazone

New England Journal of Medicine 2010;363(22):2081-2084

Shah ND, Montori VM, Krumholz HM, Tu K, Alexander GC, Jackevicius CA

Shifts in propylthiouracil and methimazole prescribing practices: Antithyroid drug use in the United States from 1991 to 2008

The Journal of Clinical Endocrinology & Metabolism 2010;95(5): 2227-2233
Emiliano AB, Governale L, Parks M, Cooper DS

Use of parenteral iron products and serious anaphylactic-type reactions

Am. J. Hematol. 2010;85(9):650-654

Wysowski DK, Swartz L, Vicky Borders-Hemphill B, Goulding MR, Dormitzer C

Impact of the allhat/jnc7 dissemination project on thiazide-type diuretic use

Arch Intern Med 2010;170(10):851-858

Stafford RS, Bartholomew L, Cushman WC, et al

Changes in US antidepressant and antipsychotic prescription patterns during a period of FDA actions

Pharmacoepidem. Drug Safe. 2010;19(2):158-174

Pamer CA, Hammad TA, Wu Y, et al

IMS INSTITUTE
FOR
HEALTHCARE INFORMATICS

IMS Institute for Healthcare Informatics, 100 IMS Drive, Parsippany, NJ 07054

info@theimsinstitute.org www.theimsinstitute.org

SELECTED HSRN ANNOTATED BIBLIOGRAPHY, 2003-2014 (Updated May 2014).

The IMS Health Services Research Network is comprised of academic researchers who are conducting empirically rigorous, policy-relevant studies to improve the quality and cost-effectiveness of health care in the United States. The network includes members from a variety of complementary disciplines including pharmacy, medicine, law, economics, business, and public policy. This annotated bibliography reflects more than 100 publications by HSRN members in the peer-reviewed literature during recent years using IMS Health's data assets.

1. Laxminarayan R, Klugman KP. Communicating trends in resistance using a drug resistance index. *BMJ Open* 2011;1:e000135 doi:10.1136/bmjopen-2011-000135.
   http://www.ncbi.nlm.nih.gov/pubmed/22102636
   The authors combined data on antibiotic use from hospital pharmacies and commercial sources with other data to develop a method for aggregating bacterial resistance to multiple antibiotics, creating an index comparable to the composite economic indices that measure consumer prices and stock market values. The use this drug resistance index (DRI) to demonstrate that composite indices that aggregate resistance to various drugs can be useful for assessing changes in drug resistance across time and space.

2. Donohue J, O'Malley AJ, Horvitz-Lennon M, Taub AL, Berndt ER, Huskamp HA. Changes in physician antipsychotic prescribing preferences, 2002-2007. Psychiatric Services. 2014;65:315-22.
   http://www.ncbi.nlm.nih.gov/pubmed/24337224
   The authors use IMS Health Xponent™ database and data on physician characteristics from the American Medical Association Masterfile to measure changes in the degree to which physicians are able to customize treatment choices in response to regulatory and payment changes. They focus on the likelihood of prescribing two first-generation antipsychotics and six second-generation antipsychotics and conduct analyses adjusted for prescribing volume, specialty, demographic characteristics, practice setting, and education. Preferences for specific antipsychotics changed dramatically during this period. Although physician prescribing remained heavily concentrated, the concentration decreased over time, particularly among psychiatrists.

3. Goldberger AD, Alexander GC. Refitting the Foxglove: Digoxin Use in Contemporary Clinical Practice. JAMA Internal Medicine. 2014;174:151-4.
   http://www.ncbi.nlm.nih.gov/pubmed/24217624
   The authors use the IMS Health National Disease and Therapeutic Index™ to quantify digoxin use from 1997 through 2012, among all subjects as well as among patient subpopulations. They find that digoxin treatment visits declined by 85.5%, from 12.9 million visits in 1997 to 1.87 million visits in 2012 (Figure 1A). Declines were greater between 1997-2001 than subsequently, and conclude that an increasing number of evidence-based therapies for heart failure, the perceived toxicities and challenges of digoxin dosing, and the negative results of the DIG trial with respect to its primary endpoint of all-cause mortality, may all have contributed to reductions in digoxin utilization.

4. Chatterjee SK, Rohrbaugh ML. NIH inventions translate into drugs and biologics with high

IMS Health
One IMS Drive
Plymouth Meeting, PA
19462
USA

Tel 610-244-2000
Fax 610-244-5007

public health impact. Nature Biotechnology. 2014;32:52–58.
http://www.ncbi.nlm.nih.gov/pubmed/24406928
The authors use data from IMS Health's MIDAS™ database to examine how NIH inventions translate into drugs and biologics with high public health impact. They conclude that compared with other US public-sector research institutions, the US National Institutes of Health has contributed inventions that have had a disproportionately greater impact on the overall number of products produced, drugs granted orphan status and drugs granted priority review.

5. Miller M, Pate V, Swanson SA, Azrael D, White A, Sturmer T. Antidepressant class, age, and the risk of deliberate self-harm: a propensity score matched cohort study of SSRI and SNRI users in the USA. CNS Drugs. 2014;28:79-88.
http://www.ncbi.nlm.nih.gov/pubmed/24146116
The authors use IMS Health LifeLink™ Health Plan Claims Database to assess the risk of deliberate self-harm associated with the two most commonly prescribed classes of antidepressant agents. Regardless of age cohort, patients initiating SSRIs and patients initiating SNRIs had similar rates of deliberate self-harm. Restriction to patients with no antidepressant use in the past 3 years did not alter our findings. They conclude that physicians who have decided that their patients would benefit from initiating antidepressant therapy need not weigh differential suicide risk when deciding which class of antidepressant to prescribe.

6. Schumock GT, Li EC, Suda KJ, Matusiak LM, Hunkler RJ, Vermeulen LC, Hoffman JM. National trends in prescription drug expenditures and projections for 2014. Am J Health Syst Pharm. 2014;71:482-99.
http://www.ashpmedia.org/AJHP/DrugExpenditures-2014.pdf
The authors use the IMS Health National Sales Perspectives™ database to analyze trends in U.S. pharmaceutical spending, including projections for drug expenditures in nonfederal hospital and clinic settings in 2014. Growth in U.S. prescription drug expenditures is expected to rebound in 2014, with a projected 3-5% increase in total drug expenditures across all settings this year, including a 5-7% increase in clinic spending and a 1-3% increase in hospital spending. They conclude that health-system pharmacy leaders should carefully examine local drug-utilization patterns to determine their respective organization's anticipated spending in 2014.

7. Han LC, Kim SP, Gross CP, Ross JS, Van Houten HK, Smaldone MC, Krambeck AE, Shah ND. Association of physician specialty and medical therapy for benign prostatic hyperplasia. Med Care. 2014;52:128-36.
http://www.ncbi.nlm.nih.gov/pubmed/24423810
The authors use IMS Health LifeLink™ Health Plan Claims Database to describe the prescribing patterns of new and existing agents among patients with incident BPH after the introduction of several new agents and determine whether these varied by physician specialty. They conclude that among insured patients diagnosed with BPH, the overall use of new agents is rising. In particular, urologists were more likely to prescribe newer selective α-1 blockers compared with PCPs.

8. May L, Klein EY, Rothman RE, Laxminarayan R. Trends in antibiotic resistance in coagulase-negative staphylococci in the United States, 1999 to 2012. Antimicrob Agents Chemother. 2014;58:1404-9.
http://www.ncbi.nlm.nih.gov/pubmed/24342646

The authors use IMS Health Xponent™ data to examine trends in antibiotic resistance in coagulase-negative staphylococci in the United States. Between 1999 and 2012, S. epidermidis resistance to ciprofloxacin and clindamycin increased steadily from 58.3% to 68.4% and from 43.4% to 48.5%, respectively. Resistance to levofloxacin increased rapidly from 57.1% in 1999 to a high of 78.6% in 2005, followed by a decrease to 68.1% in 2012. Multidrug resistance for CoNS followed a similar pattern, and this rise and small decline in resistance were found to be strongly correlated with levofloxacin prescribing patterns. The results from our study demonstrate that the antibiotic resistance in CoNS pathogens has increased significantly over the past 13 years.

9. Suda KJ, Regan SM, Lee TA, Easterling JL, Hunkler RJ, Danziger LH. Outpatient influenza antiviral prescription trends with influenza-like illness in the USA, 2008–2010. International Journal of Antimicrobial Agents. 2014;43:279-283.
http://www.sciencedirect.com/science/journal/09248579/43/3
The authors use IMS Health Xponent™ to assess antiviral geographic trends and correlation with influenza-like illness (ILI) over 3 years. A positive correlation was observed between antivirals and ILI visits ($R^2 = 0.7853$; $P < 0.0001$). With the 2009 H1N1 pandemic, antivirals increased compared with 2008 or 2010. Without the concern of H1N1, antivirals decreased in 2010 to levels lower than 2008. Geographic trends were also observed, which may be a result of the different intensity of influenza transmission and difference practice patterns. The authors conclude that ILI diagnoses correlate with influenza antiviral prescription use in the USA.

10. Dilokthornsakul P, Chaiyakunapruk N, Schumock GT, Lee TA. Calendar time-specific propensity score analysis for observational data: a case study estimating the effectiveness of inhaled long-acting beta agonist on asthma exacerbations. Pharmacoepidemiology and Drug Safety. 2013. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24150874
The authors used the IMS Health LifeLink PharMetrics Health Plan Claims Database to conduct a retrospective cohort study evaluating calendar time-specific propensity scores compared with standard non-time specific methods. There was minimal difference between the two propensity score methodologies when examining the effectiveness of inhaled long-acting beta agonists on asthma exacerbations.

11. Li S, Laxminarayan R. Are physicians' prescribing decisions sensitive to prices? Evidence from a free-antibiotics program. Health Econ. 2013. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24167098
The authors used the IMS Health Xponent database to examine the effect of cost considerations on physicians' prescribing decisions. To do so, they focused on the effect of a free-antibiotic program on retail antibiotic sales at a zip code level. There was an overall increase in antibiotic prescribing under the free program and substitutions to covered antibiotics away from non-covered antibiotics, and this effect was stronger in low-income areas, both suggesting the impact that this program had on prescribing decisions.

12. Moore TJ, Furberg CD. Development times, clinical testing, postmarket follow-up, and safety risks for the new drugs approved by the US Food and Drug Administration: the class of 2008. JAMA Internal Medicine. 2013 [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24166236
The authors used the IMS National Prescription Audit™ (NPA) to assess the appropriateness of new standards for FDA drug approval by examining the development times, clinical testing, postmarket follow-up, and safety risks for the new drugs approved by the FDA in 2008, when most provisions of current law, regulation, and policies were in effect. They conclude that new drugs approved by the FDA in 2008 that received expedited review were approved more rapidly than those that received standard review. However,

considerably fewer patients were studied prior to approval, and many safety questions remained unanswered. By 2013, many postmarketing studies had not been completed.

13. Moore, TJ. Monitoring FDA MedWatch Perspectives in this issue: Anticoagulants leading drug safety problem reported directly to FDA Three anti-TNF agents dominate manufacturer reports of new, serious injuries, Fentanyl patches (DURAGESIC) prominent in product problems and medication errors Lower limb fractures when taking alendronate (FOSAMAX) a major reported adverse event. Data from 2012 Quarter 4.
http://www.ismp.org/quarterwatch/pdfs/2012Q4.pdf
The authors used the IMS National Prescription Audit™ (NPA) to provide context for a report describing leading drug safety problems of 2012 including concerns regarding anticoagulants, anti-TNF agents, fentanyl patches and osteoporosis medications. The NPA data was used to calculate total dispensed outpatient prescriptions for these products and comparator products and the report highlights the heightened frequency and severity of adverse events associated with these products.

14. Outterson K, Powers JH, Seoane-Vazquez E, Rodriguez-Monguio R, Kesselheim AS. Approval and withdrawal of new antibiotics and other antiinfectives in the US 1980-2009. Journal of Law, Medicine & Ethics. 2013'41;688-696.
http://onlinelibrary.wiley.com/doi/10.1111/jlme.12079/abstract
The authors used the IMS MIDAS database to determine discontinuations and withdrawals of antibiotics and other anti-infectives to determine the context for the decline in the number of approvals for these products. They examined all new molecule entities (NMEs) and new biologic licenses (NBLs) approved by the FDA from 1980–2009, and compared approval rates of the 61 approved antibiotics to trends in other drug classes. There were more withdrawals for antibiotics than other drug classes. After adjusting for drugs subsequently withdrawn, they conclude that the record for antibiotic innovation was less dire than previously reported.

15. Dellon ES, Jensen ET, Martin CF, Shaheen NJ, Kappelman MD. Prevalence of eosinophilic esophagitis in the United States. Clinical Gastroenterology and Heptology. 2013 [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/24035773
The authors used the IMS Lifelink PharMetrics Health Plan Claims Database to identify cases of eosinophilic esophagitis (EoE) in order to estimate the prevalence in the US population. They found an estimated period prevalence of EoE was 56.7/100,000 persons, translating to approximately 152,000 cases in the United States.

16. Adimadhyam S, Schumock GT, Walton S, Joo M, McKell J, Lee TA. Risk of arrythmias associated with ipratopium bromide in children, adolescents, and young adult with asthma: a nested case control study. Pharmacotherapy. 2013.
http://www.ncbi.nlm.nih.gov/pubmed/23918239
The authors used the IMS LifeLink Health Plan Claims Database to gather information on a cohort of children, adolescents and young adults who where diagnosed with asthma and were new users of asthma controller medications. The goal of this study was to evaluate the risk of arrhythmias associated with inhaled anticholingergic use. Using a nested case-control design, the authors found that you patients actively using high doses of IAC had a significantly increased risk of arrhythmias.

17. Casalino LP, Wu FM, Ryan AM, Copeland K, Rittenhouse RD, Ramsay PP, Shortell SM. Independent practice associations and physician-hospital organizations can improve care management for small practices. Health Affairs. 2013;32:1376-1382.
http://www.ncbi.nlm.nih.gov/pubmed/23918481

The authors used the IMS Health Healthcare Organizational Services database to derive a nationally representative sample of 1,164 medical practices with fewer than twenty physicians. These practices were surveyed on the extent to which independent practice associations (IPAs) and physician-hospital organizations (PHOs) might make it possible for small practices to share resources and improve care. The authors found that small practices participating in these organizations provided nearly three times as many care management processes for patients with chronic conditions as nonparticipating practices. These organizations may provide a way for small and medium-sized practices to improve care and participate in accountable care organizations.

18. Moore TJ . Monitoring FDA MedWatch Perspectives in this issue: Finasteride (PROPECIA) and sexual side effects Methylphenidate (DAYTRANA) patches and product problems, Update on anticoagulants 1/10/2013 Data from 2012 Quarter 2.
http://www.ismp.org/quarterwatch/pdfs/2012Q2.pdf
The authors analyzed FDA reports of adverse events associated with methylphenidate patch. The authors used the IMS National Prescription Audit™ (NPA) to calculate total dispensed outpatient prescriptions, noting that it accounted for 3% of the ADHD market in 2012. The report highlights the heightened frequency of adverse events such as decreased appetite and mood swings associated with methylphenidate patches in contrast to other ADHD medications.

19. Hoffman JM, Li E, Doloresco F, Matusiak L, Hunkler RJ, Shah ND, Vermeulen LC, Schumock GT. Projecting future drug expenditures in U.S. nonfederal hospitals and clinics—2013. American Journal of Health-System Pharmacy. 2013; 70: e1-e15
www.ncbi.nlm.nih.gov/pubmed/23456407
The authors used IMS Health National Sales Perspectives™ database to analyze prescription drug expenditures from September 2011 through 2012. Total prescription sales in the US increased 0.8% from the previous 12 months at $326.0 billion. The rate of growth was low due to increases in new product expenditures (3.3%) and the prices of existing products (5.9%), in addition to an overall decline in volume and mix (-8.4%). Total prescription expenditures grew 2.7%, with oncology products accounting for 32.3% of drug expenditures in the clinic setting the first 9 months, and antineoplastic agents being the top expenditure in nonfederal hospitals.

20. Conti RM, Bernstein AC, Villaflor VM, Schilsky RL, Rosenthal MB. Prevalence of Off-Label Use and Spending in 2010 Among Patent-Protected Chemotherapies in a Population-Based Cohort of Medical Oncologists. Journal of Clinical Oncology. 2013; 31(9) 1134-1139
http://jco.ascopubs.org/content/31/9/1134.full.pdf+html
The authors used IMS Health National Sales Perspectives™ to examine the prevalence of off-label anticancer drug utilization, basing criteria for off-label use on the National Comprehensive Care Network (NCCN) Compendium recommendations. Seventy percent of use was on-label, while 30% was off-label and 14% of use fitted an NCCN-supported off-label indication. Ten percent of off-label use was associated with an FDA-approved cancer site but an NCCN unsupported cancer stage. Spending for chemotherapies was $12 billion. They concluded that commonly used, novel chemotherapies are more often used on-label than off-label in contemporary practice. Off-label use is composed of a roughly equal mix of chemotherapy applied in clinical settings supported by the NCCN and those that are not.

21. Kornfield R, Donohue J, Berndt ER, Alexander GC. Promotion of Prescription Drugs to Consumers and Providers, 2001–2010. PLOS One. 2013;8:1-7
http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0055504
The authors used IMS Health Integrated Promotional Services™ to examine whether pharmaceutical firms have changed promotional expenditures due to a variety of changing market forces including reductions in new product approvals, restrictions on some forms of promotion, and the expanding role of biologic therapies. Pharmaceutical promotion peaked in 2004 and had declined substantially by 2010. Direct-to-consumer advertising (DTCA) promotion similarly declined, and remains highly concentrated. Top

biologics were promoted less than top-selling small molecule therapies. Little change occurred in the composition of promotion between primary care physicians and specialists from 2001–2010.

22. Kozman D, Graziul C, Gibbons R, Alexander GC. Association between unemployment rates and prescription drug utilization in the United States, 2007–2010. BMC Health Services Research. 2012; 12: 1-8.
www.ncbi.nlm.nih.gov/pubmed/23193954
The authors combined IMS Health XponentTM from September 2007 through July 2010 with data from the Bureau of Labor Statistics to examine the association between unemployment and utilization of prescriptions of seven therapeutic classes (statins, antidepressants, antipsychotics, angiotensin-converting enzyme [ACE] inhibitors, opiates, phosphodiesterase [PDE] inhibitors and oral contraceptives) in the United States. There were no statistically significant associations between use of ACE inhibitors or SSRIs/SNRIs and average unemployment in analyses across states, while for opioids and PDE inhibitors there were small statistically significant direct associations, and for the remaining classes inverse associations. They conclude that any effects of the recent economic recession on prescription drug utilization have been mitigated by other market forces.

23. Kornfield R, Watson S, Higashi AS, Conti RM, Dusetzina SB, Garfield CF, Dorsey ER, Huskamp HA, Alexander GC. Effects of FDA Advisories On the pharmacologic Treatment of ADHD, 2004-2008. Psychiatric Services. 2013; 64(4): 339-46
www.ncbi.nlm.nih.gov/pubmed/23318985
The authors used the IMS Health National Disease and Therapeutic Index™ to assess the effect of public health advisories issued between 2005 and 2007 by the U.S. Food and Drug Administration (FDA) on treatments of attention-deficit hyperactivity disorder (ADHD) and physician prescribing practices. The authors did not find any evidence that FDA advisories regarding potential cardiovascular and other risks of ADHD medications affected the use of these medicines.

24. Huskamp HA, O'Malley AJ, Horvitz-Lennon M, Taub AL, Berndt ER, Donohue JM. How quickly do physicians adopt new drugs? The case of second-generation antipsychotics. Psychiatric Services. 2013; 64(4): 324-30
www.ncbi.nlm.nih.gov/pubmed/23280376
The authors used IMS Xponent™ and Cox proportional-hazards models to examine physician adoption of second-generation antipsychotic medications and to detect physician-level factors associated with early adoption. Doctors waited an average of two years to before prescribing new second-generation antipsychotics. General practitioners were much slower than psychiatrists to adopt second-generation antipsychotics, while solo practitioners were slower than group practitioners to adopt most products. Psychiatrists prescribed a broader set of antipsychotics than other provider types. Understanding the numerous factors that influence physicians' adoption of new medications is vital to improving value and safety.

25. Long MD, Martin C, Sandler RS, Kappelman MD. Increased risk of pneumonia among patients with inflammatory bowel disease. The American Journal of Gastroenterology. 2013;108: 240-8.
www.ncbi.nlm.nih.gov/pubmed/23295276
The authors used the IMS LifeLink™ Health Plan Claims in a retrospective cohort and a nested case–control study to determine the pneumonia risk in inflammatory bowel disease (IBD) and how specific medications affect this risk. The IBD cohort had an increased pneumonia risk when compared to non-IBD. In the nested case–control analysis, the use of biologic medications, corticosteroids, thiopurines, proton-pump inhibitor, or narcotics was independently associated with pneumonia. They concluded the patients with IBD are at increased risk for pneumonia, particularly associated with the use of corticosteroids and narcotics. Primary prevention of pneumonia through vaccination and reduction of risk factors is warranted.

26. Long MD, Farraye FA, Okafor PN, Martin C, Sandler RS, Kappelman MD. Increased risk of pneumocystis jiroveci pneumonia among patients with inflammatory bowel disease. Inflammatory Bowel Disease. 2013; 19(5): 1018-24.
www.ncbi.nlm.nih.gov/pubmed/23478805
The authors used the IMS LifeLink™ Health Plan Claims to determine the incidence and relative risk of pneumocystis jiroveci pneumonia (PCP) in inflammatory bowel disease (IBD) and to describe medication exposures in patients with IBD with PCP. The crude incidence of PCP was higher in the IBD cohort (10.6/100,000) than in the non-IBD cohort (3.0/100,000). In the adjusted analyses, PCP risk was higher in the IBD versus non-IBD cohort with the most risk in Crohn's disease when compared with non-IBD. Although the overall incidence of PCP is low, patients with IBD are at increased risk. Patients with IBD with PCP are predominantly on corticosteroids alone or in combination before PCP diagnosis. Although the overall incidence of PCP is low, patients with IBD are at increased risk.

27. Long MD, Martin C, Sandler RS, Kappelman MD. Increased risk of herpes zoster among 108 604 patients with inflammatory bowel disease. Alimentary Pharmacology & Therapeutics. 2013; 37(4): 420-9
www.ncbi.nlm.nih.gov/pubmed/23240738
The authors used the IMS LifeLink™ Health Plan Claims Database to determine the risk of herpes zoster (HZ) in inflammatory bowel disease (IBD) and how antitumour necrosis factor-alpha (anti-TNF) agents affect this risk. The IBD cohort had increased HZ risk compared with non-IBD. Risk of HZ was highest with combination anti-TNF and thiopurine therapy. Anti-TNF, corticosteroids, and thiopurines were independently associated with HZ. Patients with inflammatory bowel disease are at increased risk for herpes zoster. Use of thiopurines, anti-TNF agents, combination therapy and corticosteroids increases herpes zoster risk.

28. Herfarth HH, Long MD, Isaacs KL. Methotrexate: underused and ignored? Digestive Diseases and Sciences. 2012; 30(3): 112-8
www.ncbi.nlm.nih.gov/pubmed/23295701
The authors used the IMS LifeLink™ Health Plan Claims Database to examine the potential reasons for the underuse of methotrexate in patients with inflammatory bowel diseases (IBD). Methotrexate is underused due to reasons such as the need to be injected or that it cannot be used during pregnancy. They conclude that even though methotrexate is not often used for IBD treatment, it should be considered since it is an affordable and effective alternative for Crohn's disease therapy. The authors conclude that methorexate remains an affordable and effective treatment for Crohn's disease, especially considering its relatively low costs.

29. King M, Essick C, Bearman P, Ross JS. Medical school gift restriction policies and physician prescribing of newly marketed psychotropic medications: difference-in-differences analysis. BMJ. 2013; 346: 1-9
www.bmj.com/content/346/bmj.f264
The authors used the IMS Health's Lifelink™ LRX longitudinal prescription database to examine the effect of attending a medical school that has a policy restricting giving gifts to representatives of pharmaceutical and device industries on subsequent prescribing behavior. Newly marketed drugs and drugs in general were not prescribed as much when there was an active gift restriction policy. They concluded that exposure to a gift restriction policy during medication school was associated with reduced prescribing of two out of three newly introduced psychotropic medications.

30. King M, Essick C. The geography of antidepressant, antipsychotic, and stimulant utilization in the United States. Helth & Place. 2013; 20: 32-8
www.ncbi.nlm.nih.gov/pubmed/23357544
The authors used IMS LifeLink™ Longitudinal Prescription database to analyze the use of antidepressant, antipsychotic and stimulant medications in the United States. The use of antidepressants in three digit

postal codes ranged from less than 1% of residents to more than 40% residents. Clusters of elevated use of antidepressants, antipsychotics, and stimulants were also found in the postal codes. This geographic variation was found to be due to access to health care, insurance coverage and pharmaceutical marketing efforts. They concluded that access to health care, insurance coverage and pharmaceutical marketing efforts explain much of the geographic variation in use.

31. McClellan SR, Casalino LP, Shortell SM, Rittenhouse DR. When does adoption of health information technology by physician practices lead to use by physicians within the practice? Journal of The American Medical Informatics Association. 2013
www.ncbi.nlm.nih.gov/pubmed/23396512
The authors used the IMS Healthcare Organization Services™ database to determine the extent to which adoption of health information technology (HIT) by physician practices may differ from the extent of use by individual physicians. There was a 34.1% rate adopting any of the five HIT functionalities of the physician practices. When the HIT functionalities were adopted, one in seven physicians did not use the functionalities and one in five physicians did not use prompts and reminders following adoption by their practice They concluded that larger practices were most likely to have adopted HIT, but other factors, including specialty mix and self-reported patient-centered management, had a stronger influence on the use of HIT once adopted; however, adoption of HIT by practices does not mean that physicians will use the HIT.

32. Scheffler RM, Bowers LG. A new vision for California's healthcare system: Integrated care with aligned financial incentives. Berkeley Forum. 2013.
http://berkeleyhealthcareforum.berkeley.edu/wp-content/uploads/A-New-Vision-for-California%E2%80%99s-Healthcare-System.pdf
The authors used the IMS Health National Healthcare Organization Services™ to characterize the size of medical groups in California. More than 40% of physicians practice in medical groups of more than 25 physicians, and 80% of these physicians are in groups of more than 100. Conversely, 35% of physicians in California practice in group of less than 4. Urban areas such as San Francisco and Los Angeles have a greater percentage of large practices than suburban and rural areas. This was part of a comprehensive report on the health care system in California

33. Hicks LA, Taylor TH Jr, Hunkler RJ. U.S. outpatient antibiotic prescribing, 2010. N Engl J Med. 2013;368:1461-2.
http://www.ncbi.nlm.nih.gov/pubmed/23574140
Data on oral antibiotic prescriptions dispensed during 2010 in the United States were extracted from the IMS Health Xponent™ database. Prescriptions were totaled for 17 provider specialty groups on the basis of the self-designated specialty of the prescriber (as defined by the American Medical Association) associated with each prescription. Health care providers prescribed 258.0 million courses of antibiotics in 2010, or 833 prescriptions per 1000 persons. Penicillins and macrolides were the most common categories prescribed. The most frequently prescribed antibiotic agent was azithromycin. Prescribing rates were higher among children and the elderly. Prescribing rates varied considerably according to provider specialty.

34. Moore TJ, Cohen MR, Furberg CD. Perspectives On GLP-1 Agents for Diabetes.
www.ismp.org/QuarterWatch/pdfs/2012Q3.pdf
The authors used the Prescription Audit™ (NPA) to describe the utilization of GLP-1 agents in treating diabetes in the face of serious safety concerns. Between June 2011 and June 2012, 1,723 serious adverse drug events were reported for GLP-1 drugs, including pancreatitis, pancreatic cancer and thyroid cancer. During this same period, almost 17 million prescriptions had been dispensed for these products, led by sitagliptin, which accounted for 66% of all GLP-1 drugs.

35. Ryan AM, Bishop TF, Shih S, Casalino LP. Small Physician Practices In New York Needed Sustained Help To Realize Gains In Quality From Use Of Electronic Health Records. Health Affairs. 2013; 32: 53-62
http://content.healthaffairs.org/content/32/1/53.full.pdf+html
The authors used IMS Health Healthcare Organization Services™ 2011 data set to evaluate the early effects on quality of the Primary Information Project that provides subsidized EHRs (electronic health records) and technical assistance to primary care practices in underserved New York City neighborhoods. Quality of care was not improved if there was only a general participation in the program. Quality of care was only improved if there was a sustained level of exposure (nine or more months) to the program because of better access to EHRs.

36. Gallini A, Donohue JM, Huskamp HA. Diffusion of antipsychotics in the US and French markets, 1998-2008.
http://www.ncbi.nlm.nih.gov/pubmed/23584568
The authors used the IMS Health Xponent™ database and the French GERS database to examine trends in the adoption of second-generation antipsychotics in the US and France. Between 1998 and 2008, total antipsychotic use in the United States increased by 78%. Total use in France was consistently higher despite a 9% decrease during the period. By 2008, second-generation antipsychotics represented 86% of the antipsychotics sold in the U.S. market, versus only 40% of the French market. They concluded that there are markedly divergent trends in the diffusion of new antipsychotics in France and the United States. Some differences may be explained by differences in health systems; others may reflect physicians' preferences and norms of practice.

37. Chressanthis GA, Khedkar P, Jain N, Poddar P, Seiders MG. Generic-to-branded drug switch-back patterns: exploratory analysis and insights from the statin class. J of Pharm Health Serv Rsrch. 2011; 2:217-226
http://onlinelibrary.wiley.com/doi/10.1111/j.1759-8893.2011.00064.x/pdf
The authors used IMS Health LifeLink™ Anonymized Patient Level Data (APLD) to analyze generic-to-branded drug switch-back patterns among statin users. They found that rates of switch-backs increased with greater patient health risk such as increasing age and co-morbidities. Higher patient doses of simvastatin increased switch-back rates, from about 10% at the 5 and 10 mg doses to 16% at the 80 mg dose. Among switch-back patients, 37% had high cardiovascular risk based on the number of co-morbidities.

38. Chatterjee S, Chen H, Johnson ML, Aparasu RR. Comparative risk of cerebrovascular adverse events in community-dwelling older adults using risperidone, olanzapine and quetiapine. Drug Aging. 2012;29:807-817
http://www.ncbi.nlm.nih.gov/pubmed/23018582
The authors used the IMS LifeLink™ Health Plan Claims Database to compare the comparative risk of cerebrovascular events among community-dwelling older adults using atypical antipsychotics. After using propensity scores and adjusting for other covariates, quetiapine [hazard ratio (HR) 0.88; 95% CI 0.78, 0.99] but not risperidone (HR 1.05; 95% CI 0.95, 1.16) was associated with a decrease in the risk of cerebrovascular adverse events compared with olanzapine.

39. Kirley K, Qato DM, Kornfield R, Stafford RS, Alexander GC. National trends in oral anticoagulant use in the United States, 2007 to 2011. Circ Cardiovasc Qual Outcomes. 2012;5:615-621
http://www.ncbi.nlm.nih.gov/pubmed/22949490
The authors used the IMS Health National Disease and Therapeutic Index™ (NDTI) to quantify patterns of oral anticoagulant use among all subjects and stratified by clinical indication. They found that dabigatran has been rapidly adopted into ambulatory practice in the United States, primarily for treatment of atrial

fibrillation, but increasingly for off-label indications. They did not find evidence that dabigatran use has increased overall atrial fibrillation treatment rates.

40. Suda KJ, Hicks LA, Roberts RM, Hunkler RJ, Danziger LH. A national evaluation of antibiotic expeditures by healthcare setting in the United States, 2009. J Antimicrob Chemother. 2012; Nov 11 [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/23148204
The authors used the IMS Health National Sales Perspectives™ (NSP) to examine systemic antibiotic expenditures in 2009. The majority (61.5%) of expenditures, totaling $10.7 billion, were associated with the outpatient setting, especially from community pharmacies. Inpatient and long-term care settings accounted for 33.6% and 4.9% of expenditures, respectively. Quinolones accounted for the greatest expenditures, followed by penicillins.

41. Epstein AJ, Busch SH, Busch AB, Asch DA, Barry CL. Does exposure to conflict of interest policies in psychiatry residency affect antidepressant prescribing? Medical Care. 2013;51(2):199-203
http://www.ncbi.nlm.nih.gov/pubmed/23142772
The authors used 2009 physician-level national administrative prescribing data from IMS Health Xponent™ to determine whether exposure to Conflict of Interest (COI) policies during psychiatry residency training affects psychiatrists' antidepressant prescribing patterns after graduation. Rates of prescribing heavily promoted, brand reformulated, and brand antidepressants in 2009 were lower among post-COI graduates than pre-COI graduates at all levels of COI restrictiveness. They call for further research to assess whether these policies affect other drug classes and physician specialties similarly.

42. Graziul C, Gibbons R, Alexander GC. Association between the commercial characteristics of psychotropic drugs and their off-label use. Medical Care. 2012;50(11):940-947
http://www.ncbi.nlm.nih.gov/pubmed/23047783
The authors linked data from the IMS Health National Disease and Therapeutic Index™ (NDTI) with data from FDA@gov and the drug compendium DrugDex, to quantify the association between 4 commercial characteristics of prescription medicines and off-label use of antidepressants, antipsychotics, and mood stabilizers from 1998 through 2009. They find that drug prescription volume, rather than product age or therapeutic class age, was most strongly associated with a medicine's likelihood of off-label use. These associations were similar when examining scientifically unsupported rather than all off-label use.

43. Moore TJ, Furberg CD, Cohen MR. Finasteride (propecia, proscar) and possibly persistent sexual side effects; methylphenidate patch (daytrana) and product problems; update on anticoagualnts dabigatran (pradaxa) and rivaroxaban (xarelto). Institute for Safe Medication Practices, Horsham, PA. Published January 9, 2013. Accessed January 21, 2013.
http://www.ismp.org/quarterwatch/pdfs/2012Q2.pdf
The authors analyzed FDA reports of serious, disabling, and fatal adverse drug events in the United States in 2012, specifically analyzing signals for persistent sexual side effects reported by men who have taken finasteride for male pattern baldness or for an enlarged prostate, reviewing product problems with the methylphenidate patch used in young children to treat ADHD, and updating coverage of anticoagulant drugs with new perspectives on adverse events reported for dabigatran and rivaroxaban.

44. Moore TJ, Furberg CD, Why reports of serious adverse drug events continue to grow. Institute for Safe Medication Practices, Horsham, PA. Published October 3, 2012. Accessed January 21, 2013.
http://www.ismp.org/quarterwatch/pdfs/2012Q1.pdf

The authors analyzed FDA reports of serious, disabling, and fatal adverse drug events in the United States in 2012, specifically analyzing signals for duloxetine and serious withdrawal symptoms; pioglitazone and reported bladder cancer; aliskiren and angioedema, and rivaroxaban and thromboembolic events. The authors used the IMS National Prescription Audit™ (NPA) to calculate total dispensed outpatient prescriptions in the same time frame.

45. Laxminarayan R. Outpatient antibiotic use in the united states, 1999-2010; communicating antibiotic resistance to two common infections using a drug resistance index. http://www.cddep.org/tools/antibiotic_use_and_resistance_us_glance_1999_2010
The authors used data from IMS Health Xponent™ to examine trends in drug resistance and regional use of antibiotics between 1999 and 2010. They found that since 1999, the percentage of antibiotic prescriptions filled nationwide has dropped by 17%. However, high-consumption states are lagging in this positive trend and are seeing the smallest decrease in prescriptions, resulting in a widening use gap.

46. Hoffman JM, Li E, Doloresco, Matusiak L, Hunkler RJ, Shah ND, Vermeulen LC, Schumock GT. Projecting future drug expenditures—2012. Am J Health-Syst Pharm. 2012;69:e5-e21. http://www.ncbi.nlm.nih.gov/pubmed/22345420
The authors used data from the IMS National Sales Perspectives™ (NSP) to examine trends in total U.S. drug expenditures as well as expenditures in hospital and clinic sectors. They found that total drug expenditures increased by 2.7%, from 2009-2010, with total spending rising from $299.2 billion to $307.5 billion. Drug expenditures in clinics grew by 6.0% while hospital drug expenditures increased at the moderate rate of 1.5%. For 2012, the authors project a 3-5% increase in total drug expenditures across all settings, a 5-7% increase in expenditures for clinic-administered drugs, and a 0-2% increase in hospital drug expenditures.

47. Schumock GT, Stayner LT, Valuck RJ, Joo MJ, Gibbons RD, Lee TA. Risk of suicide attempt in asthmatic children and young adults prescribed leukotriene-modifying agents: A nested case-control study. J Allergy Clin Immunol. 2012;130:368-75. http://www.ncbi.nlm.nih.gov/pubmed/22698520
The authors used the IMS LifeLink™ Health Plan Claims Database to examine the association between use of leukotriene-modifying agents (LTMAs) and attempted suicide among asthmatic children and young adults. They found that current use of any LTMA was not associated with increased risk of a suicide attempt; in fact, the direction of effect was the opposite (adjusted odd ratio, 0.70; 95% CI, 0.36-1.39). Further research needs to be conducted to more fully understand the association between LTMAs and suicide, particularly in subpopulations.

48. Long MD, Martin CF, Pipkin CA, Herfarth HH, Sandler RS, Kappelman MD. Risk of Melanoma and Nonmelanoma Skin Cancer Among Patients With Inflammatory Bowel Disease. Gastroenterology. 2012;143:390-9. http://www.ncbi.nlm.nih.gov/pubmed/22584081
The authors used the IMS LifeLink™ Health Plan Claims Database to examine the risk of melanoma and nonmelanoma skin cancer (NMSC) among 108,579 patients with IBD from 1997 to 2009. Compared to matched controls, IBD was associated with an increased incidence of melanoma (IRR, 1.29; 95% confidence interval [CI], 1.09-1.53) and NMSC (IRR, 1.46; 95% CI, 1.40-1.53). Therapy with biologics increased the risk of melanoma (odds ratio [OR], 1.88; 95% CI, 1.08-3.29) while thiopurines increased the

risk of NMSC (OR, 1.85; 95% CI, 1.66-2.05). Patients with IBD should be counseled and monitored for skin cancer.

49. Sun L, Klein EY, Laxminarayan R. Seasonality and Temporal Correlation between Community Antibiotic Use and Resistance in the United States. Clin Infect Dis. 2012;55:687-94. http://www.ncbi.nlm.nih.gov/pubmed/22752512
The authors used the IMS Xponent™ database to study the effects of US antibiotic usage from 1999-2007 on antibiotic resistance, which was measured using data from the Surveillance Network. They found that large-scale usage of antibiotics can generate seasonal patterns of resistance that fluctuate on a short time scale with changes in antibiotic retail sales, suggesting that use of antibiotics in the winter could have a significant effect on resistance. The strong correlation between community use of antibiotics and resistance isolated in the hospital indicates that restrictions imposed at the hospital level are unlikely to be effective unless coordinated with campaigns at the community level.

50. Lichtenberg FR. The impact of pharmaceutical innovation on longevity and medical expenditure in France, 2000-2008: Evidence from longitudinal, disease-level data. NBER Working Paper.
The author used the IMS MIDAS™ database to examine the impact of pharmaceutical innovation on longevity and medical expenditures in France from 2000-2008. Using longitudinal, disease-level data, he found that the introduction of new drugs to treat a disease generally results in an increase in longevity (age at death) several years later. New drugs introduced from 1997-2005 are estimated to have reduced the number of hospital days in 2008 by about 9% over the study period and to have increased pharmaceutical expenditures in 2008 by up to 23.5%.

51. Lichtenberg FR. Pharmaceutical innovation and longevity growth in 30 developing and high-income countries, 2000-2009. NBER Working Paper No. 18235. Issued in July 2012 http://www.nber.org/papers/w18235
The author used the IMS MIDAS™ database to examine the impact of pharmaceutical innovation, as measured by the vintage of prescription drugs used, on longevity from 2000-2009. Using longitudinal, country-level data on 30 developing and high-income countries, he found that life expectancy at all ages and survival rates above age 25 increased faster in countries with larger increases in drug vintage and that the increase in drug vintage was the only variable significantly related to all measures of longevity growth. Pharmaceutical innovation is estimated to have accounted for almost three-fourths of the 1.74-year increase in life expectancy at birth in the 30 countries and for about one third of the 9.1-year difference in life expectancy at birth in 2009 between the top 5 countries and the bottom 5 countries (ranked by drug vintage in 2009).

52. Chressanthis GA, Khedkar P, Jain N, Poddar P, Seiders MG. Can Access Limits on Sales Representatives to Physicians Affect Clinical Prescription Decisions? A Study of Recent Events With Diabetes and Lipid Drugs. J Clin Hypertens. 2012;17:435-46. http://www.ncbi.nlm.nih.gov/pubmed/22747616
The authors used the IMS Healthcare Organization Services™ (HCOS) database and the IMS Xponent™ database to analyze prescribing decisions for diabetes and lipid drugs among 58,647 to 72,114 physicians. Physicians' medical practices were categorized according to the ease of access for pharmaceutical sales representatives. The authors found that physicians with lower access to representatives had slower adoption rates for a new diabetes therapy and were also slower to reduce their use of rosiglitazone following a black box warning or to switch to lipid therapy. Restricted access to

pharmaceutical representatives can both limit positive information about innovative drugs and also reduce appropriate responses to negative information about drugs.

53. Moore TJ, Furberg CD, Cohen MR. QuarterWatch: Monitoring FDA MedWatch reports: Anticoagulants the leading reported drug risk in 2011. Institute for Safe Medication Practices, Horsham, PA. Published May 31, 2012. Accessed Aug 23, 2012.
http://www.ismp.org/quarterwatch/pdfs/2011Q4.pdf
The authors analyzed FDA reports of serious, disabling, and fatal adverse drug events in the United States in 2011 and identified anticoagulants the most frequently reported suspect drugs. The authors used the IMS National Prescription Audit™ (NPA) to calculate total dispensed outpatient prescriptions in the same time frame, noting that 48% of the population was taking a prescription drug in any given month, and an estimated 3.6 billion outpatient prescriptions were dispensed.

54. Yin HS, Parker RM, Wolf MS, Mendelsohn AL, Sanders LM, Vivar KL, Carney K, Cerra ME, Dreyer BP. Health literacy assessment of labeling of pediatric nonprescription medications: Examination of characteristics that may impair parent understanding. Acad Pediatr. 2012 May 10. [Epub ahead of print].
http://www.ncbi.nlm.nih.gov/pubmed/22579032
The authors used the IMS Heath National Medicine Cabinet™ Database to identify top-selling pediatric nonprescription analgesic, cough/cold, allergy, or gastrointestinal products for the 52 weeks ending October 30, 2009. The labeling and packaging materials for 200 products were reviewed and coded for the presence and format of active ingredient information and dosing instructions. The format and content of labels for nonprescription pediatric liquid medications could be improved to facilitate parent understanding of key medication information.

55. Shih YC, Ward JF, Pettaway CA, Xu Y, Matin SF, Davis JW, Thompson BP, Elting LS. Comparative effectiveness, cost, and utilization of radical prostatectomy among young men within managed care insurance plans. Value Health. 2012;15:367-75.
http://www.ncbi.nlm.nih.gov/pubmed/22433769
The authors used the IMS LifeLink™ Health Plan Claims Database to compare utilization, clinical outcomes, and costs between two types of radical postratectomy among young patients. Between 2003 and 2007, minimally invasive prostatectomies increased from 5.7% to 50.7% of prostatectomies and were associated with fewer complications than retropubic prostatectomies. Lower costs of complications appear to have offset higher hospitalization costs of minimally invasive prostatectomy.

56. Gautier D, Lichtenberg FR. Does competition stimulate drug utilization? The impact of changes in market structure on US drug prices, marketing and utilization. International Review of Law and Economics. 2012;32:95-109.
http://www.sciencedirect.com/science/article/pii/S0144818811000585
The authors used IMS sales and promotional data to examine the relationship between drug pricing, marketing expenditures, and the demand for prescription drugs between 2000 and 2004. They found that the two effects of increased competition on utilization - positive (via price), and negative (via marketing) - almost exactly offset one another, so the net effect of patent expiration on drug utilization is zero.

57. Dorn SD, Wei D, Farley JF, Shah ND, Shaheen NJ, Sandler RS, Kappelman MD. Impact of the 2008-2009 economic recession on screening colonoscopy utilization among the insured. Clin Gastroenterol Hepatol. 2012;10:278-84.
http://www.ncbi.nlm.nih.gov/pubmed/22155558
The authors used the IMS LifeLink™ Health Plan Claims Database to determine monthly rates of screening colonoscopies before and during the 2008-2009 economic recession. During the recession, insured individuals reduced their use of screening colonoscopy compared with the 2 years before the recession began. Out-of-pocket costs were related inversely to screening use. Policies to reduce cost sharing could increase adherence to recommended preventive services such as colonoscopy examinations.

58. Downing NS, Ross JS, Jackevicius CA, Krumholz HM. Avoidance of generic competition by Abbott Laboratories' fenofibrate franchise. Arch Intern Med. 2012 Apr 9. [Epub ahead of print].
http://www.ncbi.nlm.nih.gov/pubmed/22493409
The authors used the IMS National Prescription Audit™ (NPA) to examine sales of fenofibrate between 1998 and 2010. Although generic fenofibrate has been available for almost a decade, Abbott has dominated the market by releasing a series of branded formulations. Branded reformulations cost twice as much as generic versions of fenofibrate, and their use imposes an annual cost of approximately $700 million on the US health care system. This example illustrates how current policy allows pharmaceutical companies to maintain market share using reformulations of branded medications without demonstrating the superiority of next-generation products.

59. Chatterjee S, Chen H, Johnson ML, Aparasu RR. Risk of falls and fractures in older adults using atypical antipsychotic agents: a propensity score-adjusted, retrospective cohort study. Am J Geriatric Pharmacother. 2012;10:83-94.
http://www.ncbi.nlm.nih.gov/pubmed/22306198
The authors used the IMS LifeLink™ Health Plan Claims Database to examine the risk of falls and fractures in matched cohorts of older adults taking risperdone, olanzapine, and quetiapine from July 2000 to June 2008. After adjusting for propensity scores, the Cox proportional hazards model showed no statistically significant difference accross the individual atypical agents with respect to risk of falls/fractures.

60. Garfield CF, Dorsey ER, Zhu S, Huskamp HA, Conti R, Dusetzina SB, Higashi A, Perrin JM, Kornfield R, Alexander GC. Trends in attention deficit hyperactivity disorder ambulatory diagnosis and medical treatment in the United States, 2000-2010. Acad Pediatr. 2012;12:110-6.
http://www.ncbi.nlm.nih.gov/pubmed/22326727
The authors used the IMS National Disease and Therapeutic Index™ (NDTI) to examine aggregate trends in pharmacologic treatment for ADHD in children and adolescents younger than 18 years of age. From 2000 to 2010, the number of physician outpatient visits in which ADHD was diagnosed increased 66% from 6.2 million to 10.4 million visits, with psychostimulants remaining the dominant therapy. During this period, the management of ADHD shifted away from pediatricians and towards psychiatrists (from 24% to 36% of all visits). The effects of these changing treatment patterns on children's health outcomes and their families are unknown.

61. Stafford RS. Off-label use of drugs and medical devices: A review of policy implications. Clinical Pharmacology & Therapeutics. 2012;91:920–925.

http://www.ncbi.nlm.nih.gov/pubmed/22472990
The author used the IMS National Disease and Therapeutic Index™ (NDTI) to estimate annual off-label uses for drugs where off-label use without adequate evidence was most prevalent. Total costs of off-label use were calculated using cost information from the IMS National Prescription Audit™ (NPA). Off-label use is common and can increase health care costs if newer, more costly products are chosen over less costly approved products. Policies must encourage innovation while also recognizing the societal harms associated with costly therapies for which supporting evidence of comparative effectiveness is lacking.

62. Moore TJ, Furberg CD, Cohen MR. QuarterWatch 2011 Quarter 2: Signals for fingolimod and infliximab. Institute for Safe Medication Practices, Horsham, PA. Published April 5, 2012. Accessed May 4, 2012.
http://www.ismp.org/QuarterWatch/pdfs/2011Q2.pdf
The authors used the IMS National Prescription Audit™ (NPA) to calculate total dispensed outpatient prescriptions in the 2nd quarter of 2011. While reports of serious adverse events to the FDA rose 20% over the 2nd quarter of 2010, total dispensed prescriptions increased by only 0.8% in the same time frame. The authors describe the emerging safety profile of two immunosuppressant drugs associated with risks including infections and eye damage (fingolimod) and brain infections, cancers, and liver toxicity, among others (infliximab).

63. Khan U, Nicell JA. Sewer epidemiology mass balances for assessing the illicit use of methamphetamine, amphetamine and tetrahydrocannabinol. Sci Total Environ. 2012;421-422:144-162.
http://www.ncbi.nlm.nih.gov/pubmed/22361587
The authors developed and refined methods for using wastewater mass balances to assess levels of use of illicit methamphetamine, amphetamine and tetrahydrocannabinol in several countries. The IMS Health National Sales Perspectives™ was used to identify licit utilization of relevant clinical formulations for the US. The authors identified several sewer epidemiology metabolites that can be used to track an upstream population's use of illicit drugs.

64. Pillarella J, Higashi A, Alexander GC, Conti R. Trends in use of second-generation antipsychotics for treatment of bipolar disorder in the United States, 1998-2009. Psychiatr Serv. 2012;63:83-6.
http://www.ncbi.nlm.nih.gov/pubmed/22227765
The authors used the IMS National Disease and Therapeutic Index™ (NDTI) to examine trends in the use of second-generation antipsychotics for treatment of bipolar disorder before and after the FDA's approval of olanzapine for acute manic episodes of bipolar disorder in 2000. They found that the percentage of treatment visits in which a second-generation antipsychotic was prescribed increased from 18% in 1998 to 49% in 2009. Second-generation antipsychotics including olanzapine are increasingly used for bipolar disorder, and their effectiveness compared with therapeutic alternatives merits further research.

65. Schumock GT, Gibbons RD, Lee TA, Joo MJ, Stayner LT, Valuck RJ. The Association between Leukotriene-Modifying Agents and Spontaneously Reported Suicide. Drug Information Journal. 2012;46:99-106.
http://www.dovepress.com/relationship-between-leukotriene-modifying-agent-prescriptions-dispens-peer-reviewed-article-DHPS

The authors used the IMS Xponent™ database and data from the FDA Adverse Event Reporting System from 1999 to 2009 to examine the association between prescriptions for leukotriene-modifying agents (LTMAs) and completed suicides. They found that rates of reported completed suicides associated with montelukast increased substantially following warnings issued by the FDA.

66. Moore TJ, Furberg CD, Cohen MR. QuarterWatch 2011 Quarter 1: Signals for Dabigatran and Metroclopramide. Institute for Safe Medication Practices, Horsham, PA. Published January 12, 2012. Accessed January 17, 2012.
http://www.ismp.org/QuarterWatch/pdfs/2011Q1.pdf
The authors used the IMS National Prescription Audit™ (NPA) to examine outpatient prescriptions dispensed for two drugs that were associated with adverse events in the 1st quarter of 2011, dabigatran and metroclopramine. These drugs were widely used despite their association with serious risks of bleeding in the elderly (dabigatran) and brain damage (metroclopramine). The authors also used the NPA to identify the five most widely prescribed drugs during the 1st quarter of 2011, and found that all five were generic drugs with well-known risks that had been available for many years.

67. Ross JS, Jackevicius C, Krumholz HM, Ridgeway J, Montori VM, Alexander GC, Zerzan J, Fan J, Shah ND. State Medicaid Programs Did Not Make Use Of Prior Authorization To Promote Safer Prescribing After Rosiglitazone Warning. Health Affairs. 2012;31:188-98.
http://www.ncbi.nlm.nih.gov/pubmed/22232110
The authors used the IMS Health Xponent™ database to assess prescribing of diabetes medications following the FDA's May 2007 safety warning regarding rosiglitazone. Though nearly all state Medicaid programs continued to cover rosiglitazone as a preferred drug following the warning, rosiglitazone prescribing in these states nonetheless declined. Still, prescribing rates in these programs was three to five times higher than in programs that did not provide coverage without prior authorization. State Medicaid programs missed important opportunities to promote safer, more effective prescribing in the wake of the 2007 safety warning by making full use of preferred drug lists and prior authorization programs.

68. Higashi A, Zhu S, Stafford RS, Alexander GC. National Trends in Ambulatory Asthma Treatment, 1997-2009. Journal of General Internal Medicine. 2011;12:1465-70.
http://www.ncbi.nlm.nih.gov/pubmed/21769507
The authors used the IMS National Disease and Therapeutic Index™ (NDTI) and the National Ambulatory Care Survey (NAMCS) to examine national trends in the office-based treatment of asthma between 1997 and 2009. Both datasets showed modest increases in the number of annual asthma visits over this time period. Changes in office-based treatment, including increased inhaled steroid use and increased combined steroid/long-acting β(2)-agonist use, coincided with reductions in asthma morbidity and mortality.

69. Jackevicius CA, Chou MM, Ross JS, Shah ND, Krumholz HM. Generic Atorvastatin and Health Care Costs. New England Journal of Medicine. 2011 December 14. [Epub ahead of print]
http://www.nejm.org/doi/full/10.1056/NEJMp1113112
The authors used the IMS National Prescription Audit™ (NPA) to examine past trends in statin use and to project potential future cost savings associated with the availability of generic atorvastatin. The authors estimate that generic atorvastatin will have a market share of 44% by 3 years after market entry as a result of patients switching to it from simvastatin and from Crestor. Overall cost savings from the availability of

generic atorvastatin are projected to reach $4.5 billion annually by 2014; however, Pfizer has employed aggressive business tactics to retain Lipitor's revenue, delaying the release of the first generic product and postponing substantial cost savings. Pfizer's strategies may set a new precedent for the other blockbuster drugs on the verge of losing their patents.

70. Moore T. QuarterWatch 2010 Quarter 4: Signals for Two Newly Approved Drugs and 2010 Annual Summary. Institute for Safe Medication Practices, Horsham, PA. Published October 6, 2010. Accessed December 12, 2011.
http://www.ismp.org/quarterwatch/pdfs/2010Q4.pdf
The authors used the IMS National Prescription Audit™ (NPA) to estimate outpatient prescriptions dispensed for several recently approved drugs that were associated with adverse events in the 4th quarter of 2010. In the full year 2010, new cases of serious, disabling or fatal adverse drug events reported to the U.S. Food and Drug Administration increased 21.1% over 2009, while total outpatients prescriptions increased by only 1.1%. Dalfampradine and dabigatran were both associated with high numbers of adverse event reports relative to their use, which may reflect a unique safety profile for products that are new, branded, and heavily promoted. For products with limited clinical benefits, such as dalfampradine, serious adverse event reports may tip the benefit-risk balance in an unfavorable direction.

71. Hicks LA, Chien YW, Taylor TH Jr, Haber M, Klugman KP on behalf of the Active Bacterial Core Surveillance (ABCs) Team. Outpatient Antibiotic Prescribing and Nonsusceptible Streptococcus Pneumoniae in the United States, 1996–2003. Clinical Infectious Diseases. 2011;53:631-9.
http://www.ncbi.nlm.nih.gov/pubmed/21890767
The authors used the IMS Health Xponent™ database to assess the relationship between antibiotic prescribing and nonsusceptibility among invasive pneumococcal disease (IPD) isolates. The authors found that in sites where antibiotic prescribing is high, the proportion of nonsusceptible IPD is also high, suggesting that local prescribing practices contribute to local resistance patterns.

72. Schumock GT, Gibbons RD, Lee TA, Joo MJ, Valuck RJ, Stayner LT. Relationship Between Leukotriene-Modifying Agent Prescriptions Dispensed and Rate of Suicide Deaths by County in the US. Drug, Healthcare and Patient Safety. 2011;3:47-52.
http://dovepress.com/relationship-between-leukotriene-modifying-agent-prescriptions-dispens-peer-reviewed-article-DHPS
The authors used the IMS Xponent™ prescriptions database to assess the association between leukotriene receptor-modifying agents (LTMA) prescriptions dispensed and suicide deaths at the county level. The authors found a negative within-county association between the rate of total LTMA prescriptions dispensed and the suicide rate by county. These findings provide preliminary evidence that the association between LTMA and suicide could be different (ie, reduced risk) than that which might be anticipated based on previous warnings issued by the U.S. Food and Drug Administration.

73. Atkins CY, Patel A, Taylor TH Jr, Biggerstaff M, Merlin TL, Dulin SM, Erickson BA, Borse RH, Hunkler R, Meltzer MI. Estimating Effect of Antiviral Drug Use during Pandemic (H1N1) 2009 Outbreak, United States. Emerging Infectious Diseases. 2011;17:1591-8.
http://www.ncbi.nlm.nih.gov/pubmed/21888783

The authors used the IMS Xponent™ prescriptions database to estimate the number of hospitalizations likely averted due to use of influenza neuraminidase-inhibiting antiviral drugs during the pandemic (H1N1) 2009 outbreak. The authors estimated that the ≈8.2 million filled prescriptions prevented ≈8,400-12,600 hospitalizations (on the basis of median values). They argue that public health officials should consider these estimates an indication of success of treating patients during the 2009 pandemic and a warning of the need for renewed planning to cope with the next pandemic.

74. Rhea S, Glickman S, Waller A, Williams C, Glickman L. Association of Doxycycline Prescriptions and Tick-Related Emergency Department Visits in North Carolina. Southern Medical Journal. 2011;104:653-8.
http://www.ncbi.nlm.nih.gov/pubmed/21886086
The authors used the IMS Xponent™ database to compare the seasonal frequency of doxycycline prescriptions with tick-related emergency department (ED) visits in North Carolina, and to determine if doxycycline prescriptions are associated in time with an increase in the number of ED visits for a tick-related patient complaint or a subsequent diagnosis of a tick-borne infection. They found that Doxycycline prescription use did not always correlate well with suspected tick activity in North Carolina. Doxycycline prescription use cannot necessarily be used as a surrogate measure of tick activity for infectious disease surveillance until the reasons for this variability are better understood.

75. Lichtenberg FR. Pharmaceutical Companies' Variation of Drug Prices Within and Among Countries Can Improve Long-Term Social Well-Being. Health Affairs. 2011;30:1539-44.
http://www.ncbi.nlm.nih.gov/pubmed/21821571
The author used MIDAS™ data from IMS to examine the variation in drug prices across and within counties. He found that, on average, pharmaceutical companies charge lower prices in low-income countries than in industrialized nations. Manufacturers' ability to price products differently for different markets increases their profits overall, but it is also likely to result in greater investment in research and development, and therefore in more new drugs on the market.

76. Grinols EL, Lin HC. Patent Replacement and Welfare Gains. Journal of Economic Dynamics and Control. 2011;35:1586-1604.
http://www.sciencedirect.com/science/article/pii/S0165188911000893
The authors used data from the IMS National Sales Perspectives™ (NSP) and National Prescription Audit™ (NPA) to perform simulations of patent replacement and to assess the impacts on welfare and innovation. From simulations involving four drug sectors, the authors concluded that replacing patents with an intertemporal-bounty arrangement has the potential to increase welfare in the United States through reform of pharmaceutical patents by $43.9–$194 billion in present value terms (0.3–1.3% of annual GDP). The potential to increase welfare would be higher if applied to the larger sector of drugs as a whole.

77. Rittenhouse DR, Casalino LP, Shortell SM, McClellan SR, Gillies RR, Alexander JA, Drum ML. Small and Medium-Size Physician Practices Use Few Patient Centered Medical Home Processes. Health Affairs. 2011, doi: 10.1377/hlthaff.2010.1210.
http://content.healthaffairs.org/content/early/2011/06/28/hlthaff.2010.1210.full.pdf+html
The authors used the IMS Healthcare Organization Services™ (HCOS) database to identify practices of 1 to 19 physicians, at least 60% being adult primary care providers, cardiologists, endocrinologists, and pulmonologists. Lead physicians of said practices were eligible for the National Study of Small and Medium-Sized Physician Practices, a cross sectional telephone survey conducted from July 2007 to March

2009. On average, practices used one-fifth of the patient-centered medical home processes measured. Greater use of these processes was associated with a variety of internal capabilities and external incentives faced by practices, and also was greater among larger practices, hospital owned practices and health maintenance organizations.

78. Karaca-Mandic P, McCullough JS, Siddiqui MA, Van Houten H, Shah ND. Impact of New Drugs and Biologics on Colorectal Cancer Treatment and Costs. American Journal of Managed Care. 2011;17:e160-e168.
http://jop.ascopubs.org/content/7/3S/e30s.abstract
The authors used the IMS LifeLink™ Health Plan Claims Database to identify two cohorts of privately insured patients diagnosed with colorectal cancer - those diagnosed before new treatment introduction (January to December 2002) and those diagnosed after new treatment introduction (June 2004 to May 2005). New treatment options rapidly replaced those used during the first era with FOLFOX alone increasing by 14%. The findings also demonstrated increased costs associated with the use of non-standard regimens and increases in the use of second-line therapies.

79. Mehta S, Chen H, Johnson M, Aparasu RR. Risk of Serious Cardiac Events in Older Adults Using Antipsychotic Agents. American Journal of Geriatric Pharmacotherapy. 2011;9:120-32.
http://www.ncbi.nlm.nih.gov/pubmed/21565711
The authors used the IMS LifeLink™ Health Plan Claims Database to compare the risk of cardiac events in those taking atypical versus typical antipsychotics. They focused on adults older than 50 years of age receiving antipsychotic medication from July 2011 through December 2007. There were comparable rates of serious cardiac events for each group; 11.9% in those using atypical antipsychotics and 12.4% in those using typical antipsychotics. However, using survival analyses, there was an increased risk of serious cardiovascular events for those taking typical agents.

80. Moore TJ, Furberg CD, Cohen MR. 2010 Quarter 3 Monitoring MedWatch Reports 5/19/2011 New Signals for Liraglutide, Quetiapine and Varenicline. Institute for Safe Medical Practices.
http://www.ismp.org/quarterwatch/2010Q3.pdf
The authors used IMS Health's National Prescription Audit™ (NPA) to describe the number of outpatient dispensed prescriptions for medications commonly used to treat Type 2 Diabetes in 2010. Further, they use QuarterWatch™, an independent publication that monitors all domestic, serious adverse drug events reported to the FDA, to evaluate the rates of adverse events associated with the number of dispensed prescriptions. The authors found an increase in adverse reports from manufacturers (+33%) but a decrease from healthcare professionals (-17%) in addition to a 1.3% increase in outpatient dispensed prescriptions.

81. Jackevicius CA, Tu JV, Ross JS, Ko DT, Carreon D, Krumholz HM. Use of Fibrates in the United States and Canada. JAMA. 2011;305:1217-1224.
http://www.ncbi.nlm.nih.gov/pubmed/21427374
The authors used the National Prescription Audit™ (NPA) and the CompuScript™ Audit to compare the use of fibrates and evaluate the economic implications of brand vs generic use in the United States and Canada from January 2002 through December 2009. They found that use of fibrates increased steadily in the United States, though not in Canada, despite evidence raising questions regarding the relative benefits of fibrates compared with statins. Increases in fibrate use were driven primarily by branded fenofibrate.

82. Doloresco F, Fominaya C, Schumock GT, Vermeulen LC, Matusiak L, Hunkler RJ, Shah ND, Hoffman JM . Projecting Future Drug Expenditures--2011. American Journal of Health System Pharmacy. 2011;68:e1-e12.
http://www.ajhp.org/site/Drugexpenditures_2011.pdf

The authors used National Sales Perspectives™ (NSP) and National Prescription Audit™ (NPA) to analyze drug expenditure trends in 2009 and 2010, to project drug expenditures for 2011, and to examine factors likely to influence drug expenditures. Taking into account health care reform, past trends, and other related factors, the authors predicted a 3-5% increase in drug expenditures in outpatient settings, a 4-6% increase in expenditures for clinic administered drugs, and a 1-3% increase in hospital drug expenditures.

83. Gaglio PJ, Moss N, McGaw C, Reinus J. Direct-Acting Antiviral Therapy for Hepatitis C: Attitudes Regarding Future Use. Dig Dis Sci. 2011 Feb 19. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/21336604
The authors used IMS Health Incorporated Prescriber Profile™ data to establish the number of prescriptions written to treat Hepatitis C, as well as the fraction of these written by gastroenterologists or hepatologists (55%), internal medicine physicians (11%), and nurse practitioners (8%). They used these data in a survey evaluating knowledge and attitudes towards direct-acting antiviral therapies and other treatments of Hepatitis C.

84. Alexander GC, Gallagher SA, Mascola A, Moloney RM, Stafford RS. Increasing Off-Label Use of Antipsychotic Medications in the United States, 1995-2008. Pharmacoepidemiol Drug Saf. 2011;20:177-184
http://www.ncbi.nlm.nih.gov/pubmed/21218418
The authors used the IMS National Disease and Therapeutic Index™ (NDTI) to quantify patterns of typical and atypical antipsychotic use. They document the replacement of typical with atypical agents, substantial increases in atypical use from 2000 through 2007, and an increasing use of atypical therapies for settings with uncertain scientific support.

85. Hersh AL, Stafford RS. Antiviral Prescribing by Office-Based Physicians During the 2009 H1N1 Pandemic. Ann Intern Med. 2011;154:74-6.
http://www.ncbi.nlm.nih.gov/pubmed/21200049
The authors used the IMS National Disease and Therapeutic Index™ (NDTI) to estimate the number of monthly visits in which influenza was diagnosed and the proportion of visits in which an antiviral was prescribed for influenza between October 2006 and March 2010. The authors found a surge of influenza visits and antiviral prescribing attributable to the 2009 H1N1 influenza pandemic from October to December 2009, though there was no change in the overall propensity to prescribe antivirals in ambulatory settings compared with previous years.

86. Tsai SA, Stefanick ML, Stafford RS. Trends in Menopausal Hormone Therapy Use of US Office-Based Physicians, 2000-2009. Menopause. April 2011 - Volume 18 - Issue 4 - pp 385-392
http://www.ncbi.nlm.nih.gov/pubmed/21127439
The authors used the IMS National Disease and Therapeutic Index™ (NDTI) to describe the number of physician visits in which menopausal hormone therapy was mentioned from 2001 to 2009. Overall, the authors saw a decline in use and an increase of lower dose and vaginal products, reflective of clinical recommendations.

87. Hicks LA, Suda KJ, Roberts RM, Hunkler RJ, Taylor TH, Danziger LH. Data Reveal Wide Geographic Variability in Antimicrobial Use in the United States, 2009. Poster, Infectious Disease Society of America, October, 2010.
http://idsa.confex.com/idsa/2010/webprogram/Paper3571.html and
Poster, Infectious Disease Society of America, October, 2010
The authors used National Sales Perspective™ (NSP) to document that roughly two-thirds of U.S. sales of antibiotics in 2009 were distributed via non-acute channels. Additional observations were made through the use of Xponent™: A group of Southern states exhibited inordinately high prescribing rates of all

classes of antibiotics; and states in which CDC-funded appropriate antibiotic use campaigns were in place exhibited below-average prescribing rates.

88. Hayes BL, Curtis JR, Laster A, Saag K, Tanner SB, Liu C, Womack C, Johnson KC, Fazila Khaliq, Carbone LD. Osteoporosis Care in the United States After Declines in Reimbursements for DXA. Journal of Clinical Densitometry. 2010;13:352-360.
http://www.ncbi.nlm.nih.gov/pubmed/21029972
The authors used the IMS National Prescription Audit™ to quantify the number of prescriptions for osteoporosis drugs, stratified by prescriber specialty, from 2005 to 2008. The authors found an increase in retail prescriptions for FDA approved osteoporosis drugs during 2007 to 2008 compared with 2005 to 2006.

89. Yin HS, Wolf MS, Dreyer BP, Sanders LM, Parker RM. Evaluation of Consistency in Dosing Directions and Measuring Devices for Pediatric Nonprescription Liquid Medications. JAMA. 2010;304:2595-602.
http://www.ncbi.nlm.nih.gov/pubmed/21119074
The authors used the IMS Health Medicine Cabinet™ database to determine the top selling nonprescription products and to assess the clarity and consistency of dosing directions and measuring dose devices at the time the FDA issued guidelines concerning dosage labels. They found top-selling therapies had highly variable and inconsistent measuring devices and instructions

90. Shah ND, Montori VM, Krumholz HM, Tu K, Alexander GC, Jackevicius CA. Responding to an FDA warning--Geographic Variation in the Use of Rosiglitazone. N Engl J Med. 2010;363:2081-4.
http://www.ncbi.nlm.nih.gov/pubmed/21083379
The authors used the National Prescription Audit™ and the Xponent™ database to analyze the effect of the rosiglitazone warning on regional prescribing variations. The authors observed a 70% decrease in rosiglitazone following an FDA warning, publication of a meta-analysis and associated media coverage. Additionally, they observed great geographic variation in rosiglitazone use between 2005 and 2009.

91. Hoffman JM, Doloresco F, Vermeulen LC, Shah ND, Matusiak L, Hunkler RJ, Schumock GT. Projecting Future Drug Expenditures--2010. Am J Health Syst Pharm. 2010;67:919-28.
http://www.ncbi.nlm.nih.gov/pubmed/20484216
The authors used National Sales Perspectives™ (NSP) and National Prescription Audit™ (NPA) to analyze drug expenditure trends in 2008 and 2009, to project drug expenditures for 2010, and to examine factors likely to influence drug expenditures. Taking into account health care reform, past trends, and other related factors, the authors predicted a 3-5% increase in drug expenditures in outpatient settings, 6-8% increase in expenditures for clinic administered drugs, and a 2-4% increase in hospital drug expenditures.

92. Taub AAL, Kolotilin A, Gibbons RS, Berndt ER. The Diversity of Concentrated Prescribing Behavior: An Application to Antipsychotics. NBER Working Paper No. 16823. Issued in February 2011
http://www.nber.org/papers/w16823
The authors use IMS Health Xponent™ data to evaluate physicians' use of atypical antipsychotics. Building on prior work, they construct a model of physician learning and then empirically evaluate several hypotheses. While prescribing behavior was generally quite concentrated, prescribers with greater volumes, psychiatric training, male prescribers, and older prescribers tended to have less concentrated prescribing patterns.

93. Martin-Doyle W, Essebag V, Zimetbaum P, Reynolds MR. Trends in US Hospitalization Rates and Rhythm Control Therapies Following Publication of the AFFIRM and RACE Trials. J Cardiovasc Electrophysiol. 2010 Nov 18. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/21087329
The authors used the IMS National Prescription Audit™ to examine the impact of trials comparing rate vs. rhythm control for atrial fibrillation on the use of rhythm control therapies and hospitalizations in the United States. Use of rhythm control therapies declined significantly after publication of the AFFIRM and RACE trials until 2005, when trends reversed and an increase in the use of catheter ablation for atrial fibrillation was also observed.

94. Mehta S, Chen H, Johnson ML, Aparasu RR. Risk of Falls and Fractures in Older Adults Using Antipsychotic Agents: a Propensity-Matched Retrospective Cohort Study. Drugs Aging. 2010;27:815-29.
http://www.ncbi.nlm.nih.gov/pubmed/20883062
The authors used the IMS LifeLink™ Health Plan Claims Database to examine the risk of falls and fractures in matched cohorts of older adults taking atypical and typical antipsychotics from July 2000 to December 2007. Cox regression model analysis revealed no statistically significant difference between atypical users and typical users with respect to risk of falls/fractures. However, duration of therapy with any antipsychotic medication for >90 days was significantly associated with increased risk of falls/fractures compared with <30 days of treatment. There is a need to be cautious while prescribing atypical and typical antipsychotics in older adults for long periods of time.

95. Banarjee D, Stafford RS. Lack of Improvement in Outpatient Management of Congestive Heart Failure in the United States. Arch Intern Med. 2010;170:1399-1400.
http://www.ncbi.nlm.nih.gov/pubmed/20696970
The authors used the IMS National Disease and Therapeutic Index™ (NDTI) to evaluate whether patterns of congestive heart failure medications have adopted evidence-based therapies. They found some recommended therapies to begin to decline in the mid-2000s while others reached a plateau in this same time frame.

96. Dorsey ER, Rabbani A, Gallagher SA, Conti RM, Alexander GC. Impact of FDA Black Box Advisory on Antipsychotic Medication Use. Archives of Internal Medicine. 2010;170:96-103.
http://www.ncbi.nlm.nih.gov/pubmed/20065205
The authors used the National Disease and Therapeutic Index™ (NDTI) to evaluate the impact of the 2005 FDA black box warning regarding the risks of atypical anti-psychotic use among elderly patients with dementia on the use of these agents. They found that the FDA advisory was associated with a 2% decrease in the use of atypical antipsychotics overall and a 19% decrease in use among elderly patients with dementia.

97. Stafford RS, Bartholomew LK, Cushman WC, Cutler JA, Davis BR, Dawson G, Einhorn PT, Furberg CD, Piller LB, Pressel SL, Whelton PK. Impact of the ALLHAT/JNC7 Dissemination Project on Prescribing of Thiazide-Type Diuretic Use Arch Intern Med. 2010;170:851-858.
http://www.ncbi.nlm.nih.gov/pubmed/14709576
The authors used the National Disease and Therapeutic Index™ (NDTI) and National Prescription Audit™ (NPA) to describe the impact of the ALLHAT/JNC7 Dissemination project on prescribing of thiazide-type diuretics. They found an association between ALLHAT/JNC7 academic detailing activities and increased

prescribing of thiazides, with increases highest in counties where academic detailing activity was also highest. However they found no increase in national thiazide-type diuretic use between 2004-2008.

98. Cohen A, Rabbani A, Shah N, Alexander GC. Changes in Glitazone Use Among Office-based Physicians in the U.S.,2003-2009. Diabetes Care. 2010;33:823-825
http://www.ncbi.nlm.nih.gov/pubmed/20103549
The authors used IMS Health's National Disease and Therapeutic Index™ data to describe changes in rosglitazone and pioglitazone use. They found an increase in glitazone use from 2003 to 2005 followed by a decrease of 16% in rosiglitazone and an increase of 14% in pioglitazone from 2005 to January 2007. Accompanying the FDA advisory there was a sharp decline in rosiglitazone from February 2007 to May 2008 while pioglitazone use simultaneously remained steady.

99. Outterson K. The Legal Ecology of Resistance: The Role of Antibiotic Resistance in Pharmaceutical Innovation. Cardozo Law Review. 2010;31:613-678
http://www.cardozolawreview.com/content/31-3/OUTTERSON.31-3.pdf
The author used MIDAS™ data to supplement an analysis of methods to approach three important policy questions concerning antibiotic resistance: (1) the tension between production of new antibiotics and conservation of existing drugs, (2) the relationship between resistance and innovation, and (3) the policy levers employed in the battle against antibiotic resistance.

100. Mehta S, Johnson ML, Chen H, Aparasu RR. Risk of Cerebrovascular Adverse Events in Older Adults Using Antipsychotic Agents: A Propensity-Matched Retrospective Cohort Study. J Clin Psychiatry. 2010;71:689-698.
http://www.ncbi.nlm.nih.gov/pubmed/20573328
The authors use the IMS LifeLink™ Health Plan Claims Database to compare the risk of cerebrovascular adverse events with second-generation antipsychotic users versus those taking first-generation antipsychotics in community-dwelling older adults. Using regression analysis, the authors found no significant association between the use of the first-versus second-generation antipsychotics and a risk of cerebrovascular adverse events.

101. Trusheim MR, Aitken ML, Berndt ER. Characterizing Markets for Biopharmaceutical Innovations: Do Biologics Differ from Small Molecules? Cambridge, MA: National Bureau of Economic Research, Working Paper 16014, May 2010. Forthcoming, Forum for Health Economics & Policy, 2010.
http://www.nber.org/papers/w16014.pdf
The authors generated a new database (TABITHA) using information from IMS Health MIDAS™ database, the FDA, the WHO, and the U.S. Bureau of Economic Analysis to examine clinical and commercial characteristics of biologic and small molecule products. They conclude that although therapeutic class composition is a significant determinant of clinical and commercial characteristics, the market dynamics of biologics differ substantially from those of small molecules.

102. Nyweide DJ, Weeks WB, Gottlieb DJ, Casalino LP, Fisher ES. Relationship of Primary Care Physicians' Patient Caseload With Measurement of Quality and Cost Performance. JAMA. 2009;302:2440-2450

http://www.ncbi.nlm.nih.gov/pubmed/19996399
The authors used the Healthcare Organization Services database maintained by IMS Health to determine whether primary care physicians in the same physician practice collectively see enough Medicare patients annually to detect meaningful differences between practices in ambulatory quality and cost measures. They concluded that relatively few primary care physician practices are large enough to reliably measure 10% relative differences in common measurements of quality and cost performance among fee-for-service Medicare patients.

103. Dorsey ER, Thompson JP, Dayoub EJ, George B, Saubermann LA, Holloway RG. Selegiline Shortage: Causes and Costs of a Generic Drug Shortage. Neurology. 2009;73:213-7.
http://www.ncbi.nlm.nih.gov/pubmed/19620609
The authors used National Prescription Audit™ (NPA) to evaluate prescription trends of generic selegiline and to quantify the economic impact of any drug substitution resulting from shortages of the generic drug that occurred in September 2007. They found that the societal cost of substituting generic selegiline with branded capsules was $75,000 over the first 4 months of the shortage.

104. Dorn SD, Farley JF, Hansen RA, Shah ND, Sandler RS. Direct-to-Consumer and Physician Promotion of Tegaserod Correlated With Physician Visits, Diagnoses, and Prescriptions. Gastroenterology. 2009; 137:518-524.
http://www.ncbi.nlm.nih.gov/pubmed/19445943
The authors used an Integrated Promotional Services™ database, the National Ambulatory/Hospital Medical Care Surveys (1997-2005), and IMS Health's National Prescription Audit™ to analyze the impact of direct-to-consumer advertising (DTCA) and physician promotion of tegaserod on the number of office visits for abdominal pain, constipation, and bloating; diagnoses of irritable bowel syndrome; and tegaserod prescriptions. They found a significant relationship between physician promotion, though not DTCA, and tegaserod prescribing.

105. Lichtenberg FR. Have Newer Cardiovascular Drugs Reduced Hospitalization? Evidence From Longitudinal Country-Level Data on 20 OECD Countries, 1995-2003. Health Economics. 2009;18:519-534.
http://www.ncbi.nlm.nih.gov/pubmed/18634121
The author used MIDAS™ to examine the effect of changes in the vintage distribution of cardiovascular system drugs on hospitalization and mortality. The estimates indicate that the use of newer cardiovascular drugs has reduced the average length of hospital stay and the age-adjusted cardiovascular mortality rate, but not the number of potential years of life lost due to cardiovascular disease before age 70 per 100,000 population.

106. Long MD, Porter CQ, Sandler RS, Kappelman MD. Suboptimal Rates of Cervical Testing Among Women with Inflammatory Bowel Disease. Clinical Gastroenterology and Hepatology. 2009;7:549-53.
http://www.ncbi.nlm.nih.gov/pubmed/18996498
The authors used IMS LifeLink™: Health Plan Claims data to determine cervical testing rates among women with inflammatory bowel disease (IBD) on immunosuppressant medications, and to identify risk factors associated with low screening rates. They found systematic under-screening of women with IBD.

107. Hoffman JM, Shah ND, Vermeulen LC, Doloresco F, Martin PK, Blake S, et al. Projecting Future Drug Expenditures – 2009. American Journal of Health System Pharmacy. 2009;66:237-57.
http://www.ncbi.nlm.nih.gov/pubmed/19179637
The authors used National Sales Perspectives™ (NSP) and National Prescription Audit™ (NPA) to analyze drug expenditure trends in 2007 and 2008, project drug expenditures for 2009, and examine factors likely to influence drug expenditures.

108. Duggan M, Morton FS. The Effect of Medicare Part D on Pharmaceutical Prices and Utilization. NBER Working Paper No. 13917
http://www.nber.org/papers/w13917
Duggan and colleagues use IMS data to investigate the effect of Medicare Part D on the price and utilization of branded pharmaceutical treatments from 2001 to 2006. The authors saw a total sales increase from $162.2 billion in 2001 to $223.9 billion in 2006. The authors concluded that Medicare Part D lowered pharmaceutical prices by approximately 13 percent for beneficiaries of the program.

109. Walton SM, Schumock GT, Lee KV, Alexander GC, Meltzer D, Stafford RS. Prioritizing Future Research on Off-Label Prescribing: Results of a Quantitative Evaluation. Pharmacotherapy. 2008;28:1443-1452.
http://www.ncbi.nlm.nih.gov/pubmed/19025425
The authors used the National Prescription Audit™ (NPA) and Integrated Promotional Services™ (IPS) to develop a prioritized list of individual drugs for which future research regarding off-label uses is warranted. They identified a high volume of off-label prescribing in the absence of good evidence for a substantial number of drugs, particularly antidepressants, antipsychotics, and anxiolytic-sedatives.

110. Philipson T, Berndt ER, Gottschalk AHB, Sun E. Cost-Benefit Analysis of the FDA: The Case of the Prescription Drug User Fee Acts. Journal of Public Economics. 2008;92:1306-1325.
http://web.mit.edu/cbi/publications/JPubE_Philipson.pdf
The authors used National Sales Perspectives™ (NSP) data to estimate the welfare effects of the Prescription Drug User Fee Acts (PDUFA). They found that PDUFA raised the private surplus of producers by about $7 to $11 billion and raised consumer welfare between $7 to $20 billion; thus the combined social surplus was raised by $14 to $31 billion, which is the equivalent of 140,000 to 310,000 life years.

111. Huskamp HA, Donohue JM, Koss C, Berndt ER, Frank RG. Generic Entry, Reformulations, and Promotion of SSRIs. PharmacoEconomics. 2008;26:603-16.
http://www.ncbi.nlm.nih.gov/pubmed/18563951
The authors used Integrated Promotional Services™ (IPS) to examine the relationships among promotional expenditures, generic entry, reformulation entry and new indication approval. They found that the introduction of new product formulations appears to be a common strategy for extending market exclusivity for medications facing impending generic entry. Manufacturers who introduced a reformulation before generic entry shifted most promotion dollars from the original brand to the reformulation long

before generic entry, and in some cases appeared to target a particular promotion type for a given indication.

112. Mindel JS. Amiodarone and Optic Neuropathy. American Heart Journal. 2008;156:411-13. http://www.ncbi.nlm.nih.gov/pubmed/18760119
The author used IMS LifeLink™: Health Plan Claims data and National Prescription Audit™ (NPA) in addition to FDA records and a prospective, double-maked randomized trial to show that the existing literature and evidence estimates of the incidence of amiodarone-associated optic neuropathy are too high. They are skeptical that amiodarone produces a toxic neuropathy or that it has a preventative effect on idiopathic anterior ischemic optic neuropathy and do not recommend that physicians consider it as a factor in deciding whether a patient will benefit from its use.

113. Aitken ML, Berndt ER, Cutler DM. Prescription Drug Spending Trends in the US: Looking Beyond the Turning Point. Health Affairs – Web Exclusive. 2009;28:W151-60. http://www.ncbi.nlm.nih.gov/pubmed/19088102
The authors used National Sales Perspectives™ (NSP) and National Prescription Audit™ (NPA) to document trends and identify underlying components: declines in the role of blockbuster drugs, increased importance of biologics and vaccines relative to traditional pharmaceuticals, and a changing medication mix away from those prescribed principally by primary care physicians toward those mostly prescribed by specialists.

114. Kappelman MD, Rifas-Shiman SL, Porter CQ, et. al. Direct Health Care Costs of Treatment of Crohn's Disease and Ulcerative Colitis in U.S. Children and Adults. Gastroenterology. 2008;135:1907-13. http://www.ncbi.nlm.nih.gov/pubmed/18854185
The authors used IMS LifeLink™: Health Plan Claims data to estimate the direct costs of Crohn's disease (CD) and ulcerative colitis (UC) in the US, to describe the distribution of costs among inpatient, outpatient, and pharmaceutical services, and to identify sociodemographic factors influencing these costs. They analyze claims from 87 health plans in 33 states between 2003 and 2004. They estimate that mean annual costs for CD and UC were $8265 and $5066, respectively, and costs were significantly higher for children younger than 20 years of age.

115. Alexander GC, Sehgal NL, Moloney RM, Stafford RS. National Trends in Treatment of Type 2 Diabetes Mellitus, 1994-2007. Archives of Internal Medicine. 2008;168:2088-2094. http://www.ncbi.nlm.nih.gov/pubmed/18955637
The authors used the National Disease and Therapeutic Index™ (NDTI), National Prescription Audit™ (NPA), and National Sales Perspective™ (NSP) to analyze medications prescribed between 1994-2007 for Type 2 diabetes. They also estimate total costs of diabetes treatments between 2001 and 2008. They conclude that increasingly complex and costly diabetes treatments are being applied to a growing population.

116. Gibbons RD, Brown CH, Hr K, et al. Early Evidence on the Effects of Regulators' Suicidality Warnings on SSRI Prescriptions and Suicide in Children and Adolescents. American Journal of Psychiatry. 2007;164:1356-63.
http://www.ncbi.nlm.nih.gov/pubmed/17728420
The authors used the National Prescription Audit™ (NPA) to assess whether regulatory warnings discouraged use of antidepressants in children and adolescents and whether they led to increases in suicide rates as a result of untreated depression. They found that SSRI prescriptions for youths decreased by approximately 22% in both the US and the Netherlands after the warnings were issued. In the Netherlands, the youth suicide rate increased by 49% between 2003 and 2005 and in the US, youth suicide rates increased by 14% between 2003 and 2004.

117. Valuck RJ, Libby AM, Orton HD, Morrato EH, Allen R, Baldessarini RJ. Spillover Effects on Treatment of Adult Depression in Primary Care After FDA Advisory on Risk of Pediatric Suicidality with SSRIs. American Journal of Psychiatry. 2007;164:1198-205.
http://www.ncbi.nlm.nih.gov/pubmed/17671282
The authors used IMS LifeLink™: Health Plan Claims data to examine the effects of the FDA public health advisory regarding the risk of suicidality in pediatric patients taking selective SSRIs on the treatment of adult depression in the community. They found that the advisory had a significant spillover effect into treatment of adults with depression, including a lower rate of diagnosed depression, decreased percentage of adults with new depressive episodes, and decreased percentage of depressed adults who did not receive an antidepressant.

118. Lee PP, Levin LA, Walt JG, Chiang TH, Doyle JJ, Stern LS, Dolgitser M. The Impact of Glaucoma Coding in a Large Claims Database. American Journal of Ophthalmology. 2007;143:867-70.
http://www.ncbi.nlm.nih.gov/pubmed/17452173
The authors used IMS LifeLink™: Health Plan Claims data to develop methods for investigating adherence to glaucoma medications based on analyses of patients receiving glaucoma medication between 1999 and 2005, chart review, and patient and physician interviews. They found that large pharmacy databases are vulnerable to errors (e.g., poor adherence, misidentification of newly treated patients), that adherence to glaucoma treatments is poor, and that the mean medication possession ratio (0.64) was a robust measure of adherence over time.

119. Arellano F, Wentworth CE, Arana A, Fernandez C, Paul C. Risk of Lymphoma Following Exposure to Calcineurin Inhibitors and Topical Steroids in Patients with Atopic Dermatitis. Journal of Investigative Dermatology. 2007;127:808-16.
http://www.ncbi.nlm.nih.gov/pubmed/17096020
The authors used IMS LifeLink™: Health Plan Claims data to perform a nested case-control study evaluating the association between topical immunosuppressants and lymphoma in a cohort of patients with atopic dermatitis. Conditional logistic regression analysis suggested that severity of atopic dermatitis was the main factor associated with an increased risk of lymphoma.

120. Berndt ER, Mortimer R, Bhattacharjya A, Parece A, Tuttle E. Authorized Generic Drugs, Price Competition and Consumers' Welfare. Health Affairs. 2007;26:790-799.
http://www.ncbi.nlm.nih.gov/pubmed/17485758

The authors used IMS National Sales Perspective™ and the National Prescription Audit™ data to analyze the effect of authorized generic entry on the timing of generic entry, brand-name and generic prices, and generic penetration. After the first four or five generic entrants, additional entrants appeared to have no effect on the long-run generic-to-brand price ratios.

121. Kuntze E, Ollendorf DA, et al. Reduced Mortality Rate after Intensive Statin Therapy in Managed-Care Patients. Value In Health. 2007;10:161-9.
http://www.ncbi.nlm.nih.gov/pubmed/17391425
The authors used IMS LifeLink™: Health Plan Claims data to evaluate whether intensive statin therapy in a managed-care setting produces greater clinical benefit than more moderate statin use based on analyses of adults hospitalized for coronary heart disease (CHD) between 2000 and 2003. They found that high risk CHD patients benefit from intensive statin therapy in a real-world, managed-care cohort, with a 29% reduced risk of death compared with those receiving standard therapy.

122. Hoffman JM, Shah ND, Vermeulen LC, Schumock GT, Grim P, Hunkler RJ, Hontz KM. Projecting Future Drug Expenditures – 2007. American Journal of Health System Pharmacy. 2007;64:298-314.
http://www.ncbi.nlm.nih.gov/pubmed/17244880
The authors used National Sales Perspectives™ (NSP) and National Prescription Audit™ (NPA) to analyze drug expenditure trends in 2005 and 2006, project drug expenditures for 2007, and examine factors likely to influence drug expenditures.

123. Naslund M, Black L, Eaddy M, Batiste LR. Differences in Alpha Blocker Usage Among Enlarged Prostate Patients Receiving Combination Therapy with 5 ARIs. American Journal of Managed Care. 2007;13Suppl1:S17-22.
http://www.ncbi.nlm.nih.gov/pubmed/17295601
The authors used IMS LifeLink™: Health Plan Claims data to assess the likelihood and timing of alpha blocker discontinuation in patients receiving combination therapy with dutasteride or finasteride plus an alpha blocker. Patients with an enlarged prostate who were taking an alpha blocker and 5-alpha reductase inhibitor in combination discontinued their alpha blocker 20% earlier when taking dutasteride than when taking finasteride.

124. Issa MM, Runken MC, Grogg AL, Shah MB. A Large Retrospective Analysis of Acute Urinary Retention and Prostate-Related Surgery in BPH Patients Treated with 5-Alpha Reductase Inhibitors: Dutasteride versus Finasteride. American Journal of Managed Care. 2007;13Suppl1:S10-6.
http://www.ncbi.nlm.nih.gov/pubmed/17295600
The authors used IMS LifeLink™: Health Plan Claims data to examine rates of acute urinary retention and surgery among patients age 50 or older diagnosed with benign prostatic hyperplasia (BPH) treated with 5-alpha reductase inhibitors (5ARIs). Patients treated with dutasteride were less likely to experience acute urinary retention than patients treated with finasteride (5.3% v 8.3%) and demonstrated a trend toward a lower likelihood of requiring surgery.

125. Jick SS, Jick H. The Contraceptive Patch in Relation to Ischemic Stroke and Acute Myocardial Infarction. Pharmacotherapy. 2007;27:218-20.

http://www.ncbi.nlm.nih.gov/pubmed/17253912
The authors used IMS LifeLink™: Health Plan Claims data to compare rates of stroke and acute myocardial infarction in users of the Ortho EVRA contraceptive patch with these rates in users of norgestimate-containing oral contraceptives among females aged 15-45 who had filled at least one prescription for either type of contraceptive between 2002 and 2005. Both ischemic stroke and acute myocardial infarction were rare among young women who use hormonal contraceptives, and the data provided no suggestion of an increased risk of either in users of either type of contraceptive.

126. Prescott JD, Factor S, Pill M, Levi GW. Descriptive Analysis of the Direct Medical Costs of Multiple Sclerosis in 2004 Using Administrative Claims in a Large Nationwide Database. Journal of Managed Care Pharmacy. 2007;13:44-52.
http://www.ncbi.nlm.nih.gov/pubmed/17269836
The authors used IMS LifeLink™: Health Plan Claims data to: 1) determine the average total and component direct medical costs incurred in the treatment of multiple sclerosis (MS) patients in 2004 and 2) compare MS treatment costs and cost factors in 2004 with 1995. Pharmacy costs accounted for 65% of total MS-related medical costs in 2004 and 75% of total costs for the subset of MS patients (58%) who receive at least 1 disease-modifying drug. Total annual MS-related treatment costs increased by 35% from 1995 to 2004.

127. Berndt ER, Danzon PM, Kruse GB. Dynamic Competition in Pharmaceuticals: Cross-National Evidence from New Drug Diffusion. Managerial and Decision Economics. 2007;28:231-250.
The authors use IMS Health MIDAS™ data to examine differences in treatment intensity, daily doses and expenditures across countries, assess differences in prices (per daily dose) of new vs old medicines, and report cross-country differences in the promotion of prescription drugs for antihypertensives, antidepressants and antiepileptics. They found substantial variation across classes and countries in promotion and diffusion. Relative to other countries, the United States was in the middle when comparing relative prices of old vs new drugs. Differences across therapeutic classes were particularly striking.

128. Radley D, Finkelstein S, Stafford RS. Off-Label Prescribing Among Office-Based Physicians. Archives of Internal Medicine. 2006;166:1021-1026.
http://www.ncbi.nlm.nih.gov/pubmed/16682577
The authors used the National Disease and Therapeutic Index™ (NDTI) to define prescribing patterns by diagnosis for 160 commonly prescribed drugs. They found that in 2001, there were an estimated 150 million off-label mentions among the sampled medications and that off-label use was most common among cardiac medications and anticonvulsants.

129. Stafford RS, Monti V, Furberg CD, Ma J. Long-Term and Short-Term Changes in Antihypertensive Prescribing by Office-Based Physicians in the U.S. Hypertension. 2006;48:213-8.
http://www.ncbi.nlm.nih.gov/pubmed/16785334
The authors used the National Disease and Therapeutic Index™ (NDTI) to describe both long and short-term trends in US antihypertensive prescribing from 1990 through 2004. They found that diuretics ranked among the top 3 antihypertensive drug classes through this time span and that evidence-based clinical recommendations had an impact on prescribing practices, though small.

130. Lichtenberg FR. The Impact of Increased Utilization of HIV Drugs on Longevity and Medical Expenditure: An Assessment Based on Aggregate U.S. Time-Series Data. Expert Review of Pharmacoeconomics and Outcomes Research. 2006;6:425-436.
http://www.nber.org/papers/w12406.pdf
The author used National Prescription Audit™ (NPA) in combination with the CDC's AIDS Public Information Data Set and data from AHRQ's Nationwide Inpatient Sample to estimate the medical cost per life-year gained from increased utilization of HIV drugs. Estimates imply that actual life expectancy of HIV/AIDS patients in 2001 was 13.4 years higher than it would have been if the drug utilization rate had not increased from its 1993 level, and medical cost per additional life-year is estimated to have been $17,175, widely considered cost-effective.

131. Arellano FM, Ulcickas Yood M, Wentworth CE, et al. Use of Cyclo-Oxygenase 2 Inhibitors (COX-2) and Prescription Non-Steroidal Anti-Inflammatory Drugs (NSAIDS) in UK and USA Populations: Implications for COX-2 Cardiovascular Profile. Pharmacoepidemiology and Drug Safety. 2006;15:861-872.
http://www.ncbi.nlm.nih.gov/pubmed/17086563
The authors combined IMS LifeLink™: Health Plan Claims data and The Health Improvement Network (THIN) data from the United Kingdom to describe the patterns of NSAIDS and COX-2 use between 1995-2004. Among the cohorts, COX-2 use was higher in the US (21%) than UK (16%). More COX-2 users than NSAIDS users received concomitant gastroprotective agents (GPA), corticosteroids and anti-platelet therapy, and had a history of thromboembolic events and hypertension. US patients were prescribed higher doses of both NSAIDS and COX-2.

132. Jumadilova Z, Varadharajan S, Girase P, Ollendorf DA. Retrospective Evaluation of Outcomes in Patients with Overactive Bladder Receiving Tolterodine Versus Oxybutynin. American Society of Health-System Pharmacists. 2006;63:2357-64.
http://www.ncbi.nlm.nih.gov/pubmed/17106009
The authors used IMS LifeLink™: Health Plan Claims data to assess the frequency, relative risk, resource utilization, and costs related to comorbidities associated with overactive bladder (OAB) based on analyses of patients with OAB who initiated treatment between 1/2001-12/2002. They found that treatment of OAB patients with tolterodine ER was associated with reduced frequency, relative risk, medical and pharmacy resource utilization, and incurred costs related to selected OAB-associated comorbidities compared with treatment with oxybutynin ER or oxybutynin IR.

133. Ollendorf DA, Lidsky L. Infliximab Drug and Infusion Costs Among Patients with Crohn's Disease in a Commercially-Insured Setting. American Journal of Therapeutics. 2006;13:502-6.
http://www.ncbi.nlm.nih.gov/pubmed/17122530
The authors used IMS LifeLink™: Health Plan Claims data to evaluate actual expenditures for infliximab by examining patterns of administration and reimbursement among commercially-insured patients receiving infliximab for Crohn's Disease (CD). The charged and paid amounts per vial billed averaged $927 and $583 respectively, so the true costs of administering infliximab are likely to be lower than reported for charged amounts.

134. Jick SS, Jick H. Cerebral Venous Sinus Thrombosis in Users of Four Hormonal Contraceptives: Levonorgestrel-Containing Oral Contraceptives, Norgestimate-Containing Oral Contraceptives,

Desogestrel-Containing Oral Contraceptives and the Contraceptive Patch. Contraception. 2006;74:290-292.
http://www.ncbi.nlm.nih.gov/pubmed/16982227
The authors used IMS LifeLink™: Health Plan Claims data to assess the risk of cerebral venous sinus thrombosis among women aged 15-44 years who filled at least one prescription for either the contraceptive patch or oral contraceptives. There was no evidence of an increased risk of cerebral venous sinus thrombosis in users of the contraceptive patch compared to users of levonorgestrel-containing oral contraceptives.

135. MacDougall DA, Feliu AL, Boccuzzi SJ, Lin J. Economic Burden of Deep-Vein Thrombosis, Pulmonary Embolism, and Post Thrombotic Syndrome. American Journal of Health System Pharmacy. 2006;63(20Suppl6):S5-15.
http://www.ncbi.nlm.nih.gov/pubmed/17032933
The authors used IMS LifeLink™: Health Plan Claims data to determine the direct medical costs of a deep-vein thrombosis (DVT) or pulmonary embolism (PE) patient across the entire continuum of care based on claims data analysis of patients with a DVT or PE diagnosis and patients with possible evidence of post-thrombotic syndrome between 1997 and 2004. The initial acute DVT or PE event was associated with high total healthcare costs and these costs were further increased by subsequent events such as recurrent DVT or PE and post-thrombotic syndrome.

136. Brassard P, Kezouh A, Suissa S. Antirheumatic Drugs and The Risk of Tuberculosis. Clinical Infectious Diseases. 2006;43:717-22.
http://www.ncbi.nlm.nih.gov/pubmed/16912945
The authors used IMS LifeLink™: Health Plan Claims data to quantify the rate of tuberculosis (TB) among a cohort of patients with rheumatoid arthritis (RA) and to assess whether the independent use of disease-modifying antirheumatic drugs (DMARDs) is associated with the risk of developing TB. They used conditional logistic regression in a nested case-control analysis of all subjects with 1 or more diagnoses of RA from 1998 to 2003. The use of biological and traditional DMARDs was associated with an increased risk of developing TB, mainly among noncurrent users of corticosteroids.

137. McLaughlin TP, Khandker RK, Kruzikas DT, Tummala R. Overlap of Anxiety and Depression in a Managed Care Population: Prevalence and Association with Resource Utilization. Journal of Clinical Psychiatry. 2006;67:1187-93.
http://www.ncbi.nlm.nih.gov/pubmed/16965195
The authors used IMS LifeLink™: Health Plan Claims data to characterize the diagnosis of anxiety and depression within a large managed care population and to measure the impact of having both of these conditions on treatment patterns, health care utilization, and cost. The combination of anxiety and depression was fairly common, patients with both conditions tended to have more somatic complaints, a higher incidence of antidepressant use, incur the highest utilization of medical services, and have the highest medical costs.

138. Suissa S, Bernatsky S, Hudson M. Antirheumatic Drug Use and the Risk of Acute Myocardial Infarction. Arthritis & Rheumatism. 2006;55:531-6.
http://www.ncbi.nlm.nih.gov/pubmed/16874796

The authors used IMS LifeLink™: Health Plan Claims data to assess the risk of acute myocardial infarction associated with the use of disease-modifying antirheumatic drugs (DMARDs) and other medications commonly used in rheumatoid arthritis. The use of DMARDs was associated with a reduction in acute myocardial infarction risk among patients with rheumatoid arthritis.

139. Hawkins RG, Houston MC. Is Population-Wide Diuretic Use Directly Associated With the Incidence of End-Stage Renal Disease in the United States? A Hypothesis. American Journal of Hypertension. 2006;19:565-7.
http://www.ncbi.nlm.nih.gov/pubmed/15925729
The authors used MIDAS™ along with a national databases for all-cause cardiovascular disease (CVD) mortality and stroke mortality from the National Vital Statistics Registry, and US Renal Data Service information to determine whether changes in drug use patterns are predictive of disease emergence in the US from 1980-98. Increasing annual diuretic distribution was directly associated with accelerated time-lagged growth rates of end-stage renal disease (ESRD) incidence.

140. Allen-Ramey FC, Bukstein D, Luskin A, Sajjan SG, Markson LE. Administrative Claims Analysis of Asthma-Related Health Care Utilization for Patients who Received Inhaled Corticosteroids with Either Montelukast or Salmeterol as Combination Therapy. Journal of Managed Care Pharmacy. 2006;12:310-21.
http://www.ncbi.nlm.nih.gov/pubmed/16792437
The authors used IMS LifeLink™: Health Plan Claims data to compare asthma-related health care resource utilization among a matched cohort of asthma patients between the ages of 4-55 years using inhaled corticosteroids (ICSs) plus either montelukast (MON) or salmeterol (SAL) as combination therapy for asthma. The use of ICS/MON compared with ICS/SAL resulted in similar odds of oral corticosteroid fills, decreased odds of Emergency Department visits and asthma-related hospitalizations, but higher utilization of short-acting beta-agonist (SABA) fills.

141. Suissa S, Hudson M, Ernst P. Leflunomide Use and The Risk of Interstitial Lung Disease in Rheumatoid Arthritis. Arthritis & Rheumatism. 2006;54:1435-9.
http://www.ncbi.nlm.nih.gov/pubmed/16645972
The authors used IMS LifeLink™: Health Plan Claims data to asses the risk of interstitial lung disease in patients with rheumatoid arthritis treated with leflunomide, a disease-modifying antirheumatic drug (DMARD), between 1998 and 2003. They found that reports of interstitial lung disease associated with leflunomide use were likely the result of the channeling of high-risk patients to leflunomide treatment, particularly those with a history of methotrexate use or preexisting ILD.

142. Joyce AT, Harrison DJ, Loebel AD, Carter CT, Ollendorf DA. Effect of Initial Ziprasidone Dose on Length of Therapy in Schizophrenia. Schizophrenia Research. 2006;83:285-92.
http://www.ncbi.nlm.nih.gov/pubmed/16545543
The authors used IMS LifeLink™: Health Plan Claims data to examine the effects of initial ziprasidone dose on discontinuation rates in patients 18 years or older with a diagnosis of schizophrenia or schizoaffective disorder and a ziprasidone claim between 2001 and 2003. Patients initiating ziprasidone with an initial dose of at least 120 mg/day had better medication adherence compared to those inittating at lower doses.

143. Black L, Naslund MJ, Gilbert TD Jr, Davis EA, Ollendorf DA. An Examination of Treatment Patterns and Costs of Care Among Patients with Benign Prostatic Hyperplasia. American Journal of Managed Care. 2006;12:S99-S110.
http://www.ncbi.nlm.nih.gov/pubmed/16551208
The authors used IMS LifeLink™: Health Plan Claims data to examine utilization and costs of care for benign prostatic hyperplasia (BPH)-related services in a large cohort of commercially insured persons. The sample included men age 45 and older who were newly diagnosed with BPH between 2000 and 2001. The results suggest that most patients undergo watchful waiting in the year after diagnosis, while rates of surgery and adverse events were low but costly.

144. Jick SS, Kaye JA, Russmann S, Jick H. Risk of Nonfatal Venous Thromboembolism in Women Using a Contraceptive Transdermal Patch and Oral Contraceptives Containing Norgestimate and 35 Microg of Ethinyl Estradiol. Contraception. 2006;73:223-8.
http://www.ncbi.nlm.nih.gov/pubmed/16472560
The authors used IMS LifeLink™: Health Plan Claims data to assess the risk of nonfatal venous thromboembolism (VTE) in women aged 15-44, who either started using a new transdermal contraceptive patch or norgestimate-35 oral contraceptives after 4/2002. They found that the risk of nonfatal VTE for the patch is similar to the risk for oral contraceptives (OR 0.9 with 95% CI 0.5-1.6).

145. Keating KN, Friedman HS, Perfetto EM. Moxifloxacin Versus Levofloxacin for Treatment of Acute Rhinosinusitis: A Retrospective Database Analysis of Treatment Duration, Outcomes, and Charges. Current Medical Research and Opinion. 2006; 22:327-33.
http://www.ncbi.nlm.nih.gov/pubmed/16466604
The authors used IMS LifeLink™: Health Plan Claims data to examine how labeled recommendations for duration of moxifloxacin and levofloxacin treatment of acute bacterial rhinosinusitis compared with real-world practice, and compare the failure and recurrence rates, and associated charges, based on analyses of claims searched over a 3-year period for episodes of acute rhinosinusitis treated within 5 days with moxifloxacin or levofloxacin. Shorter treatment durations seen for moxifloxacin reflected the label-recommended duration for acute rhinosinusitis, resulted in better outcomes than levofloxacin re: risk of treatment failure and recurrence, and lower total charges.

146. Hoffman JM, Shah ND, Vermeulen LC, Schumock GT, Grim P, Hunkler RJ, Hontz KM. Projecting Future Drug Expenditures – 2006. American Journal of Health System Pharmacy. 2006;63:123-38.
http://www.ncbi.nlm.nih.gov/pubmed/16390926
The authors used National Sales Perspectives™ (NSP) and National Prescription Audit™ (NPA) to analyze drug expenditure trends in 2004 and 2005, project drug expenditures for 2006, and examine factors likely to influence drug expenditures.

147. Wilensky J, Fiscella RG, Carlson AM, Morris LS, Walt J. Measurement of Persistence and Adherence to Regimens of IOP-Lowering Glaucoma Medications Using Pharmacy Claims Data. American Journal of Ophthalmology. 2006;141:S28-33.
http://www.ncbi.nlm.nih.gov/pubmed/16389058

The authors used IMS LifeLink™: Health Plan Claims data to determine persistence and adherence of glaucoma patients to therapeutic regimens of prostaglandin/prostamide-class medications to lower intraocular pressure. Overall, patients taking prostaglandin/prostamide medications had a mean adherence rate of 76%.

148. Stafford RS, Drieling R, Johns R, Ma J. National Patterns of Calcium Use in Osteoporosis. Journal of Reproductive Medicine. 2005; 11(Suppl): 885-895.
http://www.ncbi.nlm.nih.gov/pubmed/16422278
The authors used the National Disease and Therapeutic Index™ (NDTI) to determine whether the recent therapeutic dominance of bisphosphonates in osteoporosis treatment may have led calcium to be neglected as a component of effective management. They found that physician visits for osteoporosis in the US increased 4.5-fold between 1994 and 2004 and that during this time the proportion of visits in which bisphosphonates were prescribed increased from 14% to 81%, while reported calcium use fell from 43% to 23% of visits.

149. Lichtenberg FR. Pharmaceutical Innovation and The Burden of Disease in Developing Countries. Journal of Medicine and Philosophy. 2005; 30:663-90.
http://www.ncbi.nlm.nih.gov/pubmed/16396790
The author used drug launch data from MIDAS™ to analyze the relationship across diseases between pharmaceutical innovation and the burden of disease in developed and developing countries. Two analyses indicate that the amount of pharmaceutical innovation is positively related to the burden of disease in developed countries but not to the burden of disease in developing countries.

150. Lichtenberg FR. The Impact of New Drug Launches on Longevity: Evidence from Longitudinal Disease-Level Data From 52 Countries, 1982-2001. International Journal of Health Care Finance and Economics. 2005; 5:47-73.
http://www.ncbi.nlm.nih.gov/pubmed/15714263
The author used drug launch data from MIDAS™ to perform an econometric analysis of the effect of new drug launches on longevity. Under conservative assumptions, estimates imply that the average annual increase in life expectancy of the entire population resulting from new drug launches is about one week and that the incremental cost effectiveness ratio is about $6,750 – far lower than most estimates of the value of a statistical life-year.

151. Lee WC, Hoffmann MS, Arcona S, D'Souza J, Wang Q, Pashos CL. A Cost Comparison of Alternative Regimens for Treatment-Refractory Partial Seizure Disorder: An Econometric Analysis. Clinical Therapeutics. 2005;27:1629-38.
http://www.ncbi.nlm.nih.gov/pubmed/16330300
The authors used IMS LifeLink™: Health Plan Claims data to examine the economic costs associated with treatment-refractory partial seizure disorder and to compare the costs of two alternative approaches: a switch to oxcarbazepine monotherapy or the addition of another antiepileptic drug. Patients who had a drug added on were significantly more likely than those who were switched to have an emergency room visit after the failure of the initial regimen.

152. Stempel DA, McLaughlin TP, Stanford RH. Treatment Patterns for Pediatric Asthma Prior to and After Emergency Department Events. Pediatric Pulmonology. 2005;40:310-5.
http://www.ncbi.nlm.nih.gov/pubmed/16010682
The authors used IMS LifeLink™: Health Plan Claims data to describe the asthma treatment patterns in children aged 1-17 years in the year prior to and 2 months after an emergency department (ED) event. They found that an ED event results in only an incremental and transient increase in inhaled corticosteroid-containing controller treatment.

153. Joyce AT, Harrison DJ, Loebel AD, Ollendorf DA. Impact of Atypical Antipsychotics on Outcomes of Care in Schizophrenia. The American Journal of Managed Care. 2005;11:S254-61.
http://www.ncbi.nlm.nih.gov/pubmed/16180964
The authors used IMS LifeLink™: Health Plan Claims data to compare persistence, compliance, and psychiatric treatment costs in adults with schizophrenia having claims for atypical antipsychotics from 2001 through 2003. Patients initiated on ziprasidone had longer persistence, better compliance, and greater decreases in psychiatric-related costs than those initiated on other atypicals.

154. Schatz M, Leibman C. Inhaled Corticosteroid Use and Outcomes in Pregnancy. Annals of Allergy, Asthma, & Immunology. 2005;95:234-8.
http://www.ncbi.nlm.nih.gov/pubmed/16200813
The authors used IMS LifeLink™: Health Plan Claims data to examine asthma medication use and asthma-related health care use before and during pregnancy among women age 15-45 with both a pregnancy and asthma claim. They found that for patients using an inhaled corticosteroid before pregnancy, the rate of asthma-related physician visits decreased and the number of emergency room visits was unchanged after pregnancy, whereas physician and emergency room visits increased after pregnancy for patients not using an inhaled corticosteroid before pregnancy.

155. Lee WC, Arcona S, Thomas SK, Wang Q, Hoffmann MS, Pashos CL. Effect of Comorbidities on Medical Care Use and Cost Among Refractory Patients With Partial Seizure Disorder. Epilepsy & Behavior. 2005;7:123-6.
http://www.ncbi.nlm.nih.gov/pubmed/15939673
The authors used IMS LifeLink™: Health Plan Claims data to assess the effect of comorbidities on medical care use and costs among patients with partial seizure disorder who were refractory to initial antiepileptic drug monotherapy based on analyses of claims collected for adult patients treated with monotherapy between 2000 and 2002. They found that for patients refractory to initial AED monotherapy, the presence of comorbidities, especially depression, was associated with a substantial increase in medical care use and costs.

156. MacDougall C, Powell JP, Johnson CK, Edmond MB, Polk RE. Hospital and Community Fluoroquinolone Use and Resistance in Staphylococcus Aureus and Escherichia Coli in 17 US Hospitals. Clinical Infectious Diseases. 2005;41:435-40.
http://www.ncbi.nlm.nih.gov/pubmed/16028149
The authors used Xponent™ to determine whether variability in hospital percentages of fluoroquinolone-resistant E. coli and methicillin-resistant Staphylococcus aureus (MRSA) were associated with fluoroquinolone use in hospitals and their surrounding communities. They found associations between

fluoroquinolone use in hospitals and methicillin resistance in S. aureus and between fluoroquinolone use in communities and fluoroquinolone resistance in E. coli in hospitals.

157. Perfetto EM, Subedi P, Jumadilova Z. Treatment of Overactive Bladder: A Model Comparing Extended-Release Formulations of Tolterodine and Oxybutynin. American Journal of Managed Care. 2005;11(4 Suppl):S150-7.
http://www.ncbi.nlm.nih.gov/pubmed/16161388
The authors used IMS LifeLink™: Health Plan Claims data to compare 1-year total healthcare costs for patients with overactive bladder initiating treatment with extended-release formulations of tolterodine and oxybutynin: tolterodine tartrate extended-release capsules (tolterodine ER) v. extended-release oxybutynin chloride (oxybutynin ER). Tolterodine ER users had lower monthly drug and medical costs, and a total average annual cost savings of $204 per patient. Patients with overactive bladder were more likely to remain on original drug treatment taking tolterodine ER v. oxybutynin ER.

158. Varadharajan S, Jumadilova Z, Girase P, Ollendorf DA. Economic Impact of Extended-Release Tolterodine Versus Immediate- and Extended-Release Oxybutynin Among Commercially-Insured Persons with Overactive Bladder. The American Journal of Managed Care. 2005;11:S140-9.
http://www.ncbi.nlm.nih.gov/pubmed/16161387
The authors used IMS LifeLink™: Health Plan Claims data to examine levels of persistence and compliance as well as the economic impact of tolterodine ER v. oxybutynin IR or ER among commercially-insured patients with overactive bladder. Use of tolterodine ER resulted in comparable compliance to oxybutynin ER and longer duration of use relative to either form of oxybutynin.

159. Wingard JR, Wood CA, Sullivan E, Berger ML, Gerth WC, Mansley EC. Caspofungin versus Amphotericin B for Candidemia: A Pharmacoecomomic Analysis. Clinical Therapeutics. 2005;27:960-969.
http://www.ncbi.nlm.nih.gov/pubmed/16117996
The authors used National Sales Perspectives™ (NSP) to examine whether cost savings generated from the reduced rates of impaired renal function observed in a clinical trial would be enough to offset the higher acquisition cost of caspofungin relative to ampho B. They found that based only on differences in drug acquisition cost and renal toxicity, the use of caspofungin instead of ampho B in patients with candidemia may be a cost-saving strategy from a hospital's perspective.

160. Ollendorf DA, Massarotti E, Birbara C, Burgess S. Frequency, Predictors, and Economic Impact of Upward Dose Adjustment of Infliximab in Managed Care Patients with Rheumatoid Arthritis. Journal of Managed Care Pharmacy. 2005;11:383-93.
http://www.ncbi.nlm.nih.gov/pubmed/15934797
The authors used IMS LifeLink™: Health Plan Claims data to examine dosing patterns and costs among rheumatoid arthritis (RA) patients newly treated with infliximab between 2000 and 2002. They found that upward dose adjustment with infliximab was frequent and appeared to occur earlier in the drug therapy in 2002 v. 2000 and that upward dose adjustment was associated with significant increases in drug treatment costs.

161. Rajagopalan R, Iyer S, Perez A. Comparison of Pioglitazone With Other Antidiabetic Drugs for Associated Incidence of Liver Failure: No Evidence of Increased Risk of Liver Failure with Pioglitazone. Diabetes, Obesity, and Metabolism. 2005;7:161-9.
http://www.ncbi.nlm.nih.gov/pubmed/15715889
The authors used IMS LifeLink™: Health Plan Claims data to assess the incidence of liver failure in association with antidiabetic treatment using pioglitazone v. other oral antidiabetic medications. They found no evidence of increased risk of liver failure or hepatitis for patients initiating therapy on pioglitazone, compared to other oral antidiabetic agents.

162. Hoffman JM, Shah ND, Vermeulen LC, Hunkler RJ, Hontz KM. Projecting Future Drug Expenditures – 2005. American Journal of Health System Pharmacy. 2005;62:149-67.
http://www.ncbi.nlm.nih.gov/pubmed/15700889
The authors used National Sales Perspectives™ (NSP) and National Prescription Audit™ (NPA) to analyze drug expenditure trends in 2003 and 2004, project drug expenditures for 2005, and examine factors likely to influence drug expenditures.

163. Joyce AT, Iacoviello JM, Nag S, Sajjan S, Jilinskaia E, Throop D, Pedan A, Ollendorf DA, Alexander CM. End Stage Renal Disease-Associated Managed Care Costs Among Patients With and Without Diabetes. Diabetes Care. 2004;27:2829-35.
http://www.ncbi.nlm.nih.gov/pubmed/15562193
The authors used IMS LifeLink™: Health Plan Claims data to examine the direct costs of care before and after onset of end stage renal disease (ESRD) for patients with and without diabetes based on analyses of claims of patients with onset of ESRD between 1998 and 2002. The economic burden of ESRD in the year after onset is substantial, particularly among patients with diabetes.

164. Packer C, Stevens A, Cook A, Raftery J. Diffusion of Thromboysis for Acute Myocardial Infarction From 1981 to 2000 In England: Trend Analysis and Comparison With Need. International Journal of Technology Assessment in Health Care. 2004;20:531-536.
http://www.ncbi.nlm.nih.gov/pubmed/15609806
The authors use MIDAS™ to describe the adoption and take up of thrombolytic agents for acute myocardial infarction since 1980 in England and compare use with the estimated ceiling of need. They found that although there was a rapid initial uptake of thrombolysis in England, usage took 8 years to reach the ceiling of clinical need of 65% of patients with acute myocardial infarction, with many patients missing the opportunity to benefit.

165. Rajagopalan R, Rosenson RS, Fernandes AW, Khan M, Murray FT. Association Between Congestive Heart Failure and Hospitalization in Patients With Type 2 Diabetes Mellitus Receiving Treatment With Insulin or Pioglitazone: A Retrospective Data Analysis. Clinical Therapeutics. 2004;26:1400-10.
http://www.ncbi.nlm.nih.gov/pubmed/15531002
The authors used IMS LifeLink™: Health Plan Claims data to assess the congestive heart failure risk in patients with type 2 diabetes mellitus and to compare the association with CHF in those receiving pioglitazone and those receiving insulin. Pioglitazone therapy was associated with significantly lower incidence rates of CHF and inpatient hospitalization compared with insulin therapy.

166. Seftel AD, Sun P, Swindle R. The Prevalence of Hypertension, Hyperlipidemia, Diabetes Mellitus and Depression among Men with Erectile Dysfunction. Journal of Urology. 2004;171:2341-2345.
http://www.ncbi.nlm.nih.gov/pubmed/15126817
The authors used IMS LifeLink™: Health Plan Claims data to quantify the prevalence of diagnosed hypertension, hyperlipidemia, diabetes mellitus and depression in male health plan members with erectile dysfunction from 1995 to 2002. Each of the conditions was prevalent among the patients, hypertension (42%) and hyperlipidemia (42%) were the most common.

167. Stafford RS, Drieling RL, Hersh AL. National Trends in Osteoporosis Visits and Osteoporosis Treatment, 1988-2003. Archives of Internal Medicine. 2004;164:1525-1530.
http://www.ncbi.nlm.nih.gov/pubmed/15277283
The authors used the National Disease and Therapeutic Index™ (NDTI) to investigate patterns of pharmacotherapy from 1988-2003 and the impact of new medications on identification and treatment of patients with osteoporosis. They found that new medications for osteoporosis offering improved efficacy and convenient dosing were associated with increased frequency of patient visits and treatment.

168. Guda NM, Vakil N. Proton Pump Inhibitors and The Time Trends for Esophageal Dilation. American Journal of Gastroenterology. 2004;99:797-800.
http://www.ncbi.nlm.nih.gov/pubmed/15128339
The authors used the computerized databases of two large community hospitals and National Prescription Audit™ (NPA) data to determine the time trends for upper endoscopy and stricture dilation before and after the availability of proton pump inhibitors from 1986 through 2001. The need for stricture dilation peaked in 1994 (from 4% of patients in 1989 to 6% in 1994), and has declined thereafter, corresponding to an increase in the use of proton pump inhibitors. However, the need for esophageal dilation has not been abolished.

169. Hoffman JM, Shah ND, Vermeulen LC, Hunkler RJ, Hontz KM. Projecting Future Drug Expenditures – 2004. American Journal of Health System Pharmacy. 2004;61:145-58.
http://www.ncbi.nlm.nih.gov/pubmed/14750400
The authors used National Sales Perspectives™ (NSP) and National Prescription Audit™ (NPA) to analyze drug expenditure trends since 2002, project drug expenditures for 2004, and examine factors likely to influence drug expenditures.

170. Ollendorf D, Joyce A, Rucker M. Rate of New-Onset Diabetes Among Patients Treated With Atypical or Conventional Antipsychotic Medications for Schizophrenia. Medscape General Medicine. 2004;6:1-12.
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1140712/
The authors used IMS LifeLink™: Health Plan Claims data to compare the rates of new-onset diabetes mellitus between patients treated for schizophrenia with atypical or conventional antipsychotics. Patients with schizophrenia treated with atypical antipsychotics had a moderately increased risk of diabetes relative to those treated with conventional antipsychotics, as measured by Cox proportional hazard models (hazard ratio [HR] = 1.17, 95% confidence interval [CI] = 1.06, 1.30).

171. Stafford RS, Furberg CD, Finkelstein SN, Cockburn IM, Alehegn T, Ma J. Impact of Clinical Trial Results on National Trends of Alpha Blockers Prescribing Trends, 1996-2002. Journal of the American Medical Association. 2004;291:54-62.
http://www.ncbi.nlm.nih.gov/pubmed/14709576
The authors used the National Prescription Audit™ (NPA), National Disease and Therapeutic Index™ (NDTI), IMS market research reports, and a random sample of pharmacies and mass merchandise and discount houses to examine the changes in the prescription of alpha blockers for hypertension treatment before and after the April 2000 publication of the unfavorable Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). There were modest yet statistically significant declines in the use of doxazosin and other alpha blockers that coincided with the early termination of the ALLHAT doxazosin arm.

172. Valuck RJ, Libby AM, Sills MR, Giese AA, Allen RR. Antidepressant Treatment and Risk of Suicide Attempt by Adolescents With Major Depressive Disorder: A Propensity-Adjusted Retrospective Cohort Study. CNS Drugs. 2004; 18:1119-32.
http://www.ncbi.nlm.nih.gov/pubmed/15581382
The authors used IMS LifeLink™: Health Plan Claims data to examine the potential empirical link between antidepressant treatment and suicide attempts among adolescents aged 12-18 years. They found that antidepressant medication use had no statistically significant effect on the likelihood of suicide attempt after propensity adjustment for treatment allocation and controlling for other factors.

173. Donohue JM, Berndt ER, Rosenthal M, Epstein AM, Frank RG. Effects of Pharmaceutical Promotion on Adherence to Guideline Treatment of Depression. Medical Care. 2004;42:1176-1185.
http://www.ncbi.nlm.nih.gov/pubmed/15550797
The authors used IMS Health Integrated Promotions Services™ and MarketScan medical claims database to analyze the impact of consumer- and physician- directed marketing of antidepressants on the likelihood of being prescribed an antidepressant for a new episode of depression and the duration of antidepressant treatment. Direct-to-consumer advertising (DTCA) had a significant impact on the odds of prescription receipt while free samples had no effect.

174. Majumdar SR, Almasi EA, Stafford RS. Promotion and Prescribing of Hormone Therapy After Report by the Women's Health Initiative. 2004;292:1983-88.
http://www.ncbi.nlm.nih.gov/pubmed/15507584
The authors used data from IMS Health's National Prescription Audit™ (NPA) and Integrated Promotional Services™ (IPS), in conjunction with Consumer Media Reports to describe promotional expenditures before and after the publication of the Women's Health Initiative trial in July 2002. The authors found a 32% decrease in hormone therapy prescriptions within nine months of the publication and a decrease in all promotional activities examined.

175. McLaughlin T, Geissler EC, Wan GJ. Comorbidities and Associated Treatment Charges in Patients With Anxiety Disorders. Pharmacotherapy. 2003;23:1251-6.
http://www.ncbi.nlm.nih.gov/pubmed/14594343
The authors used IMS LifeLink™: Health Plan Claims data to describe comorbidities and treatment charges in patients receiving initial anxiolytic therapy for anxiety disorders. Many chronic conditions

were commonly associated with anxiety disorders, with hypertension the most common non-psychiatric comorbidity (22%) and depression the most common psychiatric comorbidity (37%). Treatment charges were significantly higher for patients diagnosed with an anxiety disorder.

ATTACHMENT 2

USING MOBILE PHONE ACTIVITY FOR DISASTER MANAGEMENT DURING FLOODS

PARTNERS: GOV. OF MEXICO, UN WORLD FOOD PROGRAMME, TELEFONICA RESEARCH, UNIVERSIDAD POLITECNICA DE MADRID

PROGRAMME AREA: HUMANITARIAN ACTION

SUMMARY

Natural disasters affect hundreds of millions of people worldwide every year. Emergency response efforts depend on the availability of timely information, such the movement and communication behaviours of affected populations. As such, analysis of Call Detail Records (CDRs) collected by mobile phone operators reveal new, real-time insights about human behaviour during such critical events. In this study, mobile phone activity data was combined with remote sensing data to understand how people communicated during severe flooding in the Mexican state of Tabasco in 2009, in order to explore ways that mobile data can be used to improve disaster response. By comparing the mobile data with official population census data, the representativeness of the research was validated. The results of the study showed that the patterns of mobile phone activity in affected locations during and after the floods could be used as indicators of (1) flooding impact on infrastructure and population and (2) public awareness of the disaster. These early results demonstrated the value of a public-private partnership on using mobile data to accurately indicate flooding impacts in Tabasco, thus improving early warning and crisis management.

MOBILE DATA FOR DISASTER MANAGEMENT

The lack of timely, accurate information about movement and communications of affected populations during natural disasters can limit the effectiveness of humanitarian response. However, the growing ubiquity of mobile phones has revealed new opportunities for accessing such information. Real-time mobile phone data can provide valuable insights about the behaviour of affected populations during a disaster. For example, recent research has demonstrated the potential of mobile phone data to help model malaria outbreaks in Kenya (Wesolowski et al., 2012) and study population movements after an earthquake in Haiti. (Lu et al., 2011)

By examining mobile phone activity data before, during and after a disaster, a baseline understanding of emergency behaviour and capacity to measure the rate of disaster recovery can be established. This research explored how mobile data can be used to understand the impact of floods on human behaviour using the 2009 floods in Tabasco, Mexico, as a case study.

A MULTIDISCIPLINARY CONSORTIUM

Starting on 31 October 2009, the state of Tabasco received four days of record-breaking rainfall (800mm, which was four times the November average). The resultant floods affected more than 200,000 people, and the state lost over USD 190 million in property damage.

Access to timely data about how the floods were affecting the population would have been useful in allocating emergency supplies, understanding where to target public warnings and how people were responding to the flooding.

Global Pulse worked with the Government of Mexico and several cross-sector partners to explore the potential of mobile data to provide such real-time information and access contextual information such as ground truth data from the Tabasco region, civil protection information and census data. Expert partners in data analysis and humanitarian aid were engaged to execute the project.

Telefonica Research, division of a major telecommunications company in Mexico, collaborated with data scientists from the Technical University of Madrid to conduct research under the guidance of Global Pulse and with expert advice from the UN World Food Programme (WFP) specialists on humanitarian programmes and remote sensing.

USING CALL RECORDS TO UNDERSTAND REACTIONS TO FLOODS

This study used mobile phone data combined with remote sensing data (satellite images), rainfall data, census and civil protection data. The data was provided by local mobile network operators in the form of Call Detail Records (CDRs), which are digital records of phone transactions. CDRs are generated when a phone connected to the mobile network makes or receives a phone call, or uses a service such as SMS.

The data used in the study covered the geographical area affected by the floods—Tabasco and part of Veracruz state—for nine months (July 2009 to March 2010). In order to protect customers' privacy, the CDRs were aggregated and anonymised.

Regional mobile phone activity during the Tabasco floods was compared with a baseline level of activity calculated with data collected the month prior to the floods from the same cell phone towers. Variation in the numbers of calls during floods compared to the baseline helped to show how affected populations behave in response to flooding.

OUTCOMES & INSIGHTS

This research demonstrated that mobile phone data has the potential to provide real-time information on human behaviour for improved emergency management and humanitarian response.

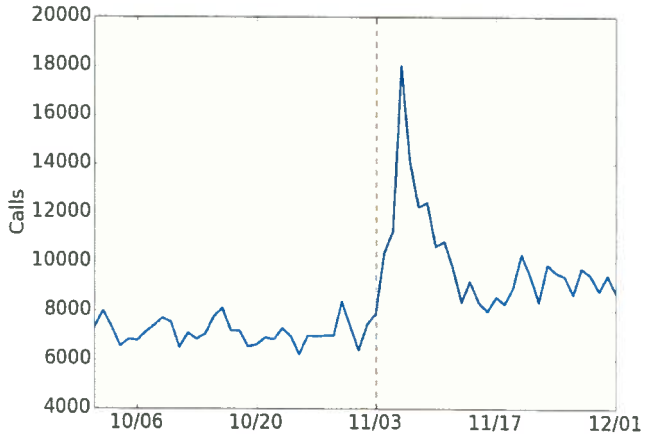
HOW TO CITE THIS DOCUMENT:

UN Global Pulse, "Using Mobile Phone Activity for Disaster Management During Floods," 2014.

Insights gained from CDR analysis could also serve as a potential proxy indicator for flood impact and risk awareness.

Several specific insights emerged from the study:

- **Mobile phone data can be highly representative of the population:** The results of the CDR study were compared with the population distribution data from the 2010 census to measure the representativeness of the sample analysed using CDRs. The comparison showed a strong linear relation between official population statistics and population estimates based on CDR data. This validation shows the possibility of using mobile phone data as a proxy indicator of population in areas where other data sources are not available or reliable.
- **Civil protection warnings are not necessarily an effective way to raise awareness:** A civil protection warning was issued on the day of highest rainfall. One might expect such a warning to boost communications activity, but big spikes in activity were only observed in two cell phone towers along the most affected road (both also suffered power outages soon after the warning was issued, making the finding somewhat inconclusive). This result did show that emergency warnings did not cause a significant increase in communication activity in the affected areas.
- **Mobile activity can provide signals of flooding impact:** In the cell phone towers that did not show a spike in mobile activity during the emergency warning (which would indicate people making calls to spread the alert), the delay between highest rainfall and peak mobile activity was typically four days. This could mean that people communicated more as a result of the initial impacts of flooding, while the civil protection warning did not generate similar levels of awareness. This finding reveals important behavioural insights for emergency responders on how and when affected populations are made aware of a disaster.
- **The most calls were made from the most impacted areas:** When analysed against the baseline activity, it was found that cell phone towers with higher variations in the number of calls made during the floods were located in the most affected locations. (For the sake of comparison, on Christmas there were similar variations in activity compared to the baseline, but across the entire Tabasco region as opposed to specific locations.) This shows that the population does communicate more than usual in the wake of a disaster.



CONCLUSIONS

The research findings demonstrated that real-time data on flood risk and public awareness is obtainable through CDRs, and could be a beneficial source of information for both emergency management and resilience assessment.

Analysing mobile activity during floods could be used to potentially locate damaged areas, efficiently assess needs and allocate resources (for example, sending supplies to affected areas). Identifying cell phone towers in the most affected areas of flooding might also serve to improve and target public communications and safety alerts, as well as help measure the effectiveness of such early warning announcements.

While it is clear that there is a need for further exploration and development of the methods used in this study, operationalizing data-driven decision making requires institutional capacities, policy frameworks and technological infrastructure that may not be in place within local or national disaster management offices.

Further research is recommended to explore how long it takes for mobile activity to stabilize and return to normal levels after a disaster, as a potential indicator of the rate of recovery for resilience measurement. It could also add dimension to decision makers' understanding of vulnerability and behaviour to combine analysis of CDRs with crowdsourced data from disaster-affected communities (for example, by conducting phone surveys via SMS).

IMPLICATIONS & RECOMMENDATIONS

- Aggregated and anonymised mobile phone data can be used to assess risk awareness, understand the effect of public communications such as disaster alerts and measure the direct impact of floods.
- It is recommended that a more extensive validation of the results be conducted by examining other incidents covering similar disasters in other geographies.
- Assessment of how information provided by mobile phone data could be integrated with the current standard information flows used during emergency response is recommended.
- The study evidenced the potential value of public-private partnerships for mobile data sharing. Therefore it is recommended that a public-private partnership framework for mobile data sharing be developed that could be used in future emergency situations.

REFERENCES

Bengtsson L, Xin Lu, Thorson A, Garfield R, von Schreeb J (2011) Improved response to disasters and outbreaks by tracking population movements with mobile phone network data: a post-earthquake geospatial study in Haiti, PLoS Medicine 8(8).

Wesolowski A, Eagle N , Tatem A, Smith D, Noor A, Snow R, Buckee C (2012) Quantifying the impact of human mobility on Malaria, Science 338(6104) 267-270.

THE FULL TECHNICAL REPORT ON THIS STUDY IS AVAILABLE:

"Flooding through the Lens of Mobile Phone Activity." Pastor-Escuredo, D., Morales-Guzmán, A. et al, IEEE Global Humanitarian Technology Conference, GHTC 2014.

ATTACHMENT 3

October 2013

GLOBAL PULSE

MOBILE PHONE NETWORK DATA FOR DEVELOPMENT

How analysis of Call Detail Records (CDRs) provides valuable information for humanitarian development action

WHAT ARE CDRs?

Whenever a mobile phone call or transaction is made, a Call Detail Record (CDR) is automatically generated by the mobile network operator. CDRs are a digital record of the attributes of a certain instance of a telecommunication transaction (such as the start time or duration of a call), but not the content. If you pay a monthly bill for your mobile phone services, take a look at the itemized list of calls: these are essentially CDRs.

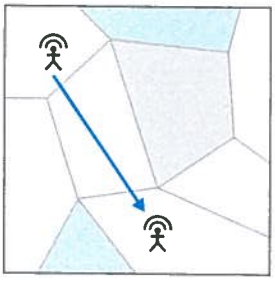
An additional piece of information that gets recorded in CDRs by a mobile network operator is to which cell towers the caller and recipient's phones were connected at the time of the call. Because the mobile network operator knows the locations of their cell towers, it is possible to use CDRs to approximate the location of both parties. The spacing of cell towers, and thus the accuracy in determining the caller's location, varies according to expected traffic and terrain. Cell towers are typically spaced 2-3km apart in rural areas and 400-800m apart in densely populated areas. This geospatial information is extremely useful for humanitarian and development applications.

HOW TO CITE THIS DOCUMENT: United Nations Global Pulse (October 2013) Mobile Phone Network Data for Development.

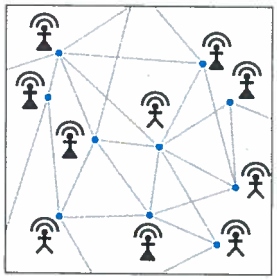
Internally, mobile phone companies use CDRs as the basis for billing customers and maintenance of their business, but CDRs can also serve other functions. Social scientists, researchers and public sector organizations have begun to research additional applications of CDRs. CDRs stored by a carrier have the potential to reveal personal information, so the records need to be altered in several important ways before being shared with third parties for analysis. First, all personally identifiable information must be removed. Typically, this is accomplished by encrypting the phone numbers of both caller and recipient. In many cases, the data from multiple callers may be aggregated to reduce risk of re-identification. Finally, data is often processed to contain the latitude and longitude from the cell tower closest to where the calls were placed. Consequently, by the time CDRs are shared, they look something like this:

CALLER ID	CALLER CELL TOWER LOCATION	RECIPIENT PHONE NUMBER	RECIPIENT CELL TOWER LOCATION	CALL TIME	CALL DURATION
X76VG588RLPQ	2°24' 22.14", 35°49' 56.54"	A81UTC93KK52	3°26' 30.47", 31°12' 18.01"	2013-11-07T15:15:00	01:12:02

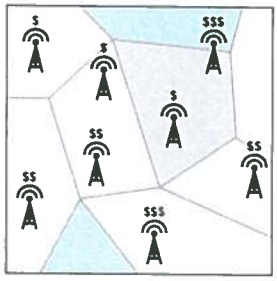
While at first glance it is difficult to assess the value of this rather rudimentary data, remarkably useful information on human behavior may be derived from large sets of de-identified CDRs. There are at least three dimensions that can be measured:



1. **MOBILITY:** As mobile phone users send and receive calls and messages through different cell towers, it is possible to "connect the dots" and reconstruct the movement patterns of a community. This information may be used to visualize daily rhythms of commuting to and from home, work, school, markets or clinics, but also has applications in modeling everything from the spread of disease to the movements of a disaster-affected population.



2. **SOCIAL INTERACTION:** The geographic distribution of one's social connections may be useful both for building demographic profiles of aggregated call traffic and understanding changes in behavior. Studies have shown that men and women tend to use their phones differently, as do different age groups. Frequently making and receiving calls with contacts outside of one's immediate community is correlated with higher socio-economic class.



3. **ECONOMIC ACTIVITY:** Mobile network operators use monthly airtime expenses to estimate the household income of anonymous subscribers in order to target appropriate services to them through advertising. When people in developing economies have more money to spend, they tend to spend a significant portion of it on topping off their mobile airtime credit. Monitoring airtime expenses for trends and sudden changes could prove useful for detecting the early impact of an economic crisis, as well as for measuring the impact of programmes designed to improve livelihoods.

CDR RESEARCH EXAMPLES

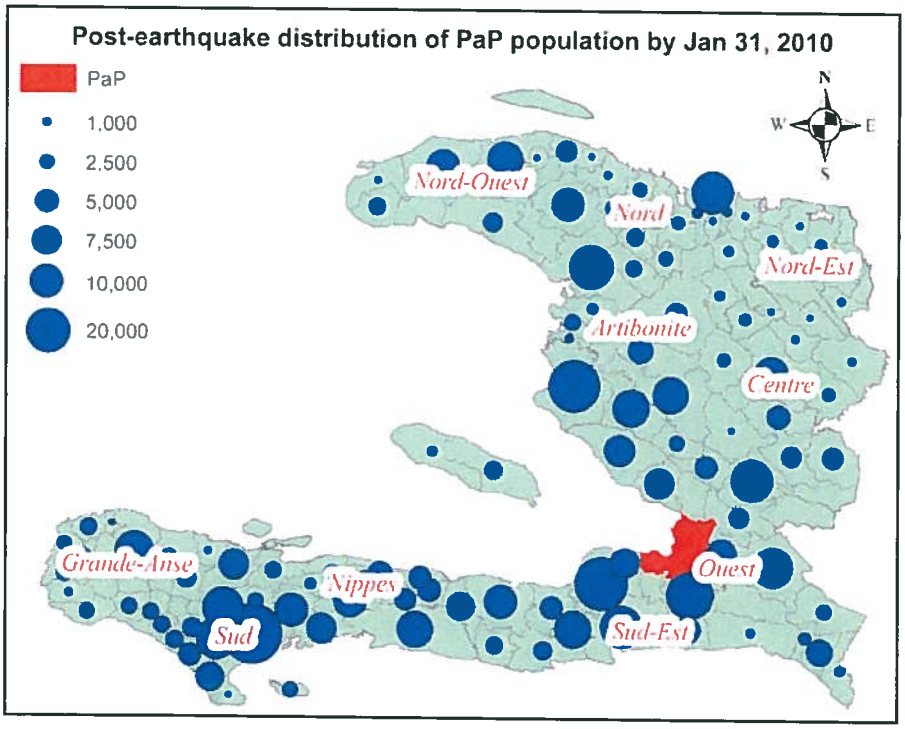
1. DISASTER RESPONSE

EMERGENCY MIGRATION IN HAITI

Natural disasters give rise to emergency situations where providing time-sensitive information is crucial for fast allocation of resources, which aids the response and recovery process. In 2010, a research team led by Sweden's Karolinska Institute showed that CDRs can be used to direct emergency aid by analyzing mobile phone records covering the time period when people are fleeing natural disasters (Bengtsson et al., 2011).

After the Haitian earthquake in 2010, many people moved away from the capital city, Port Au Prince. Researchers asked Digicell, Haiti's biggest mobile phone operator, to share de-identified information about the cell towers that subscribers were using when making calls. The data included the position of 1.9 million subscriber identity modules (SIMs) in Haiti from 42 days before the earthquake to 158 days afterwards, allowing researchers to compare people's movement in the days preceding and following the earthquake. This study proved more accurate in measuring the number of displaced people and their destinations than the studies by the Haitian Civil Protection Agency, and the estimates of geographical distribution of people across Haiti were matched by estimates from a retrospective United Nations Population Fund study.

A follow-up study (Lu et al., 2012) found that the destinations of people who left the capital during the first three weeks after the earthquake were correlated with the locations to which they had significant social bonds. This research has shown that in the event of another natural disaster, population movement patterns may be significantly more predictable than has been previously understood. This type of analysis could be used to plan relief efforts more precisely.



Mobility patterns have been identified by analyzing CDRs, providing more accurate post-analysis of population migration during the Haiti earthquake.

Figure 1: The visualization shows the distribution of population migration from Port au Prince (PaP) after the Haiti earthquake obtained by analyzing CDRs. The circles represent locations that received at least 500 people from the estimated distribution of those in PaP on the day of the earthquake, but outside the city 19 days after the earthquake. Source: Lu et al., 2012.

2. HEALTH

MAPPING MALARIA IN KENYA

Malaria kills about one million people each year. In sub-Saharan Africa, 90% of malaria-related deaths are of children under five years old (Harvard School of Public Health, 2012). When an Anopheles mosquito bites an infected person, a small amount of blood infected with microscopic malaria parasites is withdrawn. When the mosquito bites someone else, the parasite is injected with the bite, and the transmission of malaria is complete, resulting in further spread of malaria. Therefore, to predict malaria's geographic spread, it is important to factor in not only information about the location of the mosquitoes that carry the malaria parasite, but also the behavior of people who might be infected.

Researchers analyzed mobile phone data to study the regional travel patterns of nearly 15 million mobile phone subscribers in Kenya, over the course of a year (Wesolowski et al., 2012). They estimated the daily locations of 14.8 million Kenyan mobile phone subscribers between June 2008 and June 2009, mapping calls and texts to one of the towers located within the boundaries of 692 settlements. The researchers analyzed the mobile phone data together with a simple malaria transmission model based on infection prevalence data, and in doing so were able to map routes of malaria parasite dispersal. The study included people who became infected after residing in areas where the disease broke out, and those who visited areas with outbreaks, became infected and returned home. After analyzing the CDR data and using the transmission model, scientists were able to map the specific locations where malaria outbreaks originated, and the locations where the disease had a higher probability of spreading. They found that a large proportion of "imported" infections—for example, infections that are carried by people moving from one place to another—end up in Nairobi, with infected residents returning there after journeys to hot spots such as Lake Victoria.

The study indicates that assessing connectivity among different regions of Kenya can help estimate costs for regional elimination strategies, identify 'source' regions and pinpoint anticipated hot spots. These hot spots can then be targeted with use of insecticides, drugs and bed-nets and with measures such as reducing stagnant water and destruction of old tires. On a broader scale, this analysis can be used to identify the high-volume human traffic between regions that increases transmission rates, and then communicate risks to travelers to alter their behaviors, restrict travel and employ surveillance mechanisms in high-risk areas.

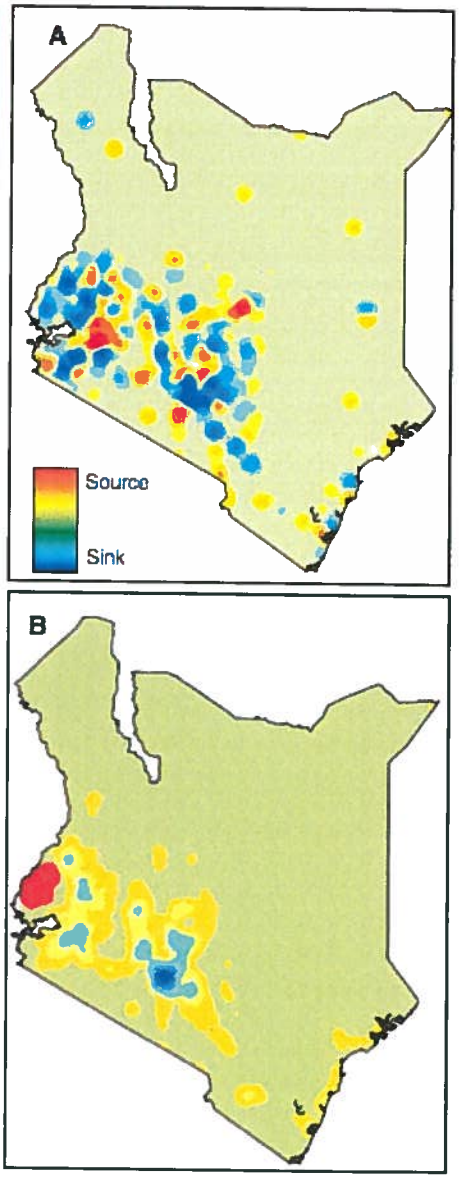


Figure 2: Figure shows sources and sinks of human travel and parasites. Kernel density maps show ranked sources (red) and sinks (blue) of human travel (2A) and total parasite movement (2B) in Kenya, where each settlement was designated as a relative source or sink based on yearly estimates. Source: Wesolowski et al., 2012.

By analyzing the regional travel patterns of millions of mobile subscribers, researchers were able to map the specific locations to which malaria had a higher probability of spreading.

COMBATING H1N1 FLU IN MEXICO

To control the spread of the H1N1 flu epidemic in 2009, the Mexican government imposed mobility restrictions on citizens. Understanding and quantifying the effect of such restrictions had not been adequately studied on a large scale before. Researchers measured the impact of the policies taken by the government to limit human mobility, using CDRs from one million anonymized customers in one of the most H1N1-affected Mexican states (Frias-Martinez et al., 2012). The data covered a period of January to May 2009. The government issued alerts in three stages: a medical alert (stage one), closing schools and universities (stage two) and suspension of all non-essential activities (stage three). It was found that up to 80% of the population reduced their mobility during stages two and three. However, the analysis also revealed an increase in the number of visitors to the airport before the suspension of all non-essential activities (stage three). This behavior might have limited the containment causing an undesired spread of the epidemic. Despite this, the results indicated that the mandates managed to reduce the peak number of individuals infected by the virus and postponed the peak of the pandemic by two days, allowing authorities to react faster to control the epidemic.

Quantitative analysis of CDR data allowed researchers to measure the effectiveness of government mandates on people's mobility during H1N1 outbreak in Mexico.

H1N1

H1N1, or swine flu, is a potentially fatal subtype of the human influenza virus. H1N1 was the source of a worldwide pandemic in 2009, including in the United States and Mexico.

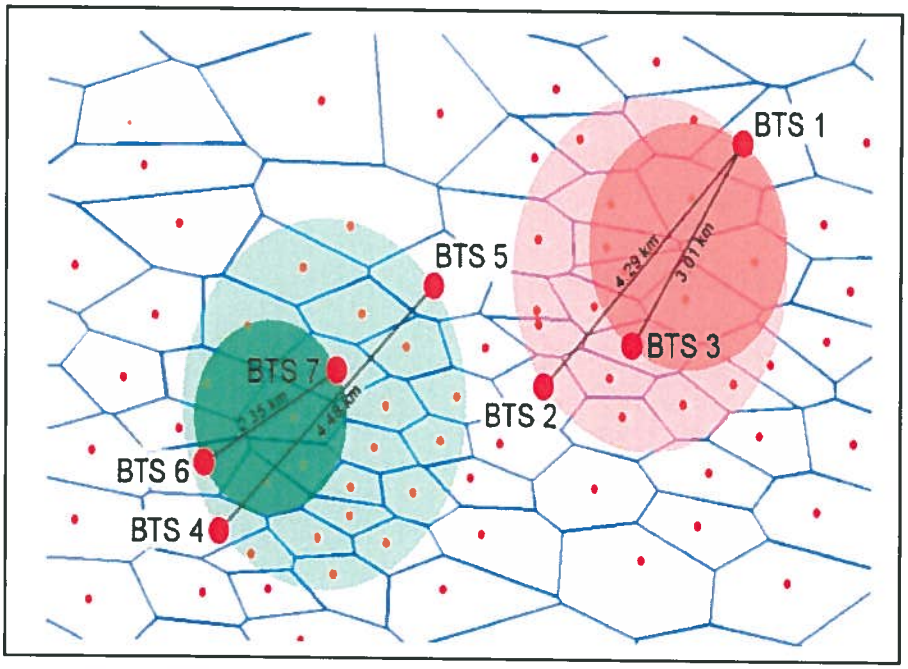


Figure 3: The visual shows the geographical region where the daily activities of an individual take place—the area of influence—for two individuals (one marked in green and the other in red). The bigger circles represent the mobility behavior under normal circumstances and the smaller circles represent the mobility behavior under the epidemic alert period. The red dots represent mobile tower stations (labeled BTS). In the case of the region marked with red, the baseline diameter of mobility is 4.29km (defined by BTS1 and BTS2). During the alert period, the diameter is reduced to 3.01km (the distance between BTS1 and BTS3). For the region marked in green, the baseline period has a diameter of 4.48km (defined by BTS4 and BTS5), and for the alert period the diameter is reduced to 2.35km (defined by BTS6 and BTS7). Source: Frias-Martinez et al., 2012.

3. SOCIO-ECONOMICS

UNDERSTANDING SOCIO-ECONOMIC INDICATORS IN THE UK

Prior studies have shown that economic opportunities are likely to come from contacts outside of tightly-knit local social groups. However, the correlation between network diversity and a population's economic well-being had not previously been quantified. To better understand this relationship, researchers studied CDRs for August 2005 in the UK (Eagle et al., 2010). The data contained over 90% of the country's mobile phones and almost 100% of the residential and business landlines. Researchers coupled this data with census information on socio-economic well-being from the UK Government's Index of Multiple Deprivation. The findings revealed that the diversity of individuals' relationships is strongly correlated with the economic development of communities. Researchers were able to validate a central assumption that was untested at the population level: that more diverse ties correlate with better access to social and economic opportunities. Although further research is needed, this valuable insight is particularly relevant to policymakers engaged in targeted poverty reduction initiatives.

Figure 4: This is an image of regional communication diversity and socioeconomic ranking for England. Communities with diverse communication patterns were found to rank higher (represented from light blue to dark blue) than the regions with more insular communication. This implies that communication diversity is a key indicator of an economically healthy community. Source: Eagle et al., 2010.

PROVIDING PROXY CENSUS MAPS IN LATIN AMERICA

This study (Frias-Martinez V, Virsesa, 2012), like the previous example regarding socio-economics in the UK (Eagle et al., 2010), focuses on socio-economic factors and their relationship to cell phone usage in Latin America. Researchers at Telefonica Research in Spain studied whether specific gender, age or socio-economic groups use mobile phones in different ways, using a new analytical approach that combined CDRs with countrywide census data gathered by the National Statistical Institute. The data set contained five months of CDRs from over ten million subscribers across twelve cities. Results showed a strong correlation between the socio-economic level of a person and the expenses, reciprocity of communications, physical distance with his/her contacts and the geographical areas around which people move. The study was also able to provide a method to approximate socio-economic indicators from calling patterns, which could provide an affordable tool in the context of resource-constrained economies.

ESTIMATING POVERTY LEVELS IN CÔTE D'IVOIRE

In another study (Smith et al., 2012), researchers used CDRs to map poverty levels in Côte d'Ivoire. No full survey of the country's population has been published since a civil war in the 1990s. Researchers used anonymized CDRs of five million Orange telecommunications customers between December 2011 and April 2012 to assess both the level of activity among subscribers and locations where calls were made. Higher levels of mobile communication and wider range of calls are a proxy indicator for prosperity. Using this data, poverty levels of eleven regions of Côte d'Ivoire were quantified. The estimate was validated when compared with a multi-dimensional poverty index created by University of Oxford, which uses indicators such as poor health, lack of education, inadequate living standard and threat from violence among other factors. This research validated the possibility of making poverty maps using CDRs.

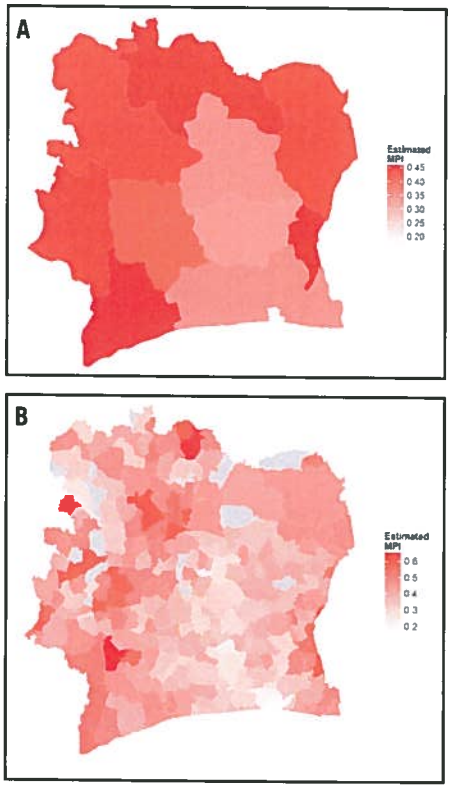


Figure 5. Figure 5A shows poverty map estimated based on the antennas in the eleven major regions of Cote d'Ivoire, where the darker areas indicate higher estimated poverty level. Figure 5B shows the Department poverty levels as approximated by the model used on regional level indicating the finer granularity possible when using CDRs. Source: Smith et al., 2012.

The previous three studies show that in countries where information regarding census, socioeconomic levels or poverty indicators is lacking, CDRs may be used to estimate these variables on an ongoing basis, thus augmenting and complementing survey data.

CDRs can provide a proxy indicator for assessing regional poverty levels, and can valuably augment national surveys in estimating changes associated with a growing economy.

4. TRANSPORTATION

OPTIMIZING TRANSPORT NETWORKS IN ABIDJAN

Rapid urbanization in developing countries has increased pressure on infrastructure such as road networks. Roads and public transportation systems become saturated, and people lose a great deal of time traveling from home to work, which in turn has a collective cost on the burgeoning economies. Researchers at IBM's AllAboard project have shown it is possible to monitor citizens' travel routes and use data-driven insights to better plan and manage transportation services (Berlingerio et al., 2013). The data analyzed included CDRs shared by Orange for 500,000 users over a five month period, which were used to pinpoint locations based on cell towers used when making calls or using a mobile-based service. The researchers studied CDR data, mapped against 85 bus routes in Abidjan, Ivory Coast's largest city, where the bus transport network spans 539 buses, 5,000 mini-buses and 11,000 shared taxis. Their findings allowed the researchers to suggest a partial solution to the city's congestion: add four routes to Abidjan's existing infrastructure and extend another route. This optimized network would reduce travel time by 10%. Such a provisioning method using CDRs would be useful for better urban planning and public transportation.

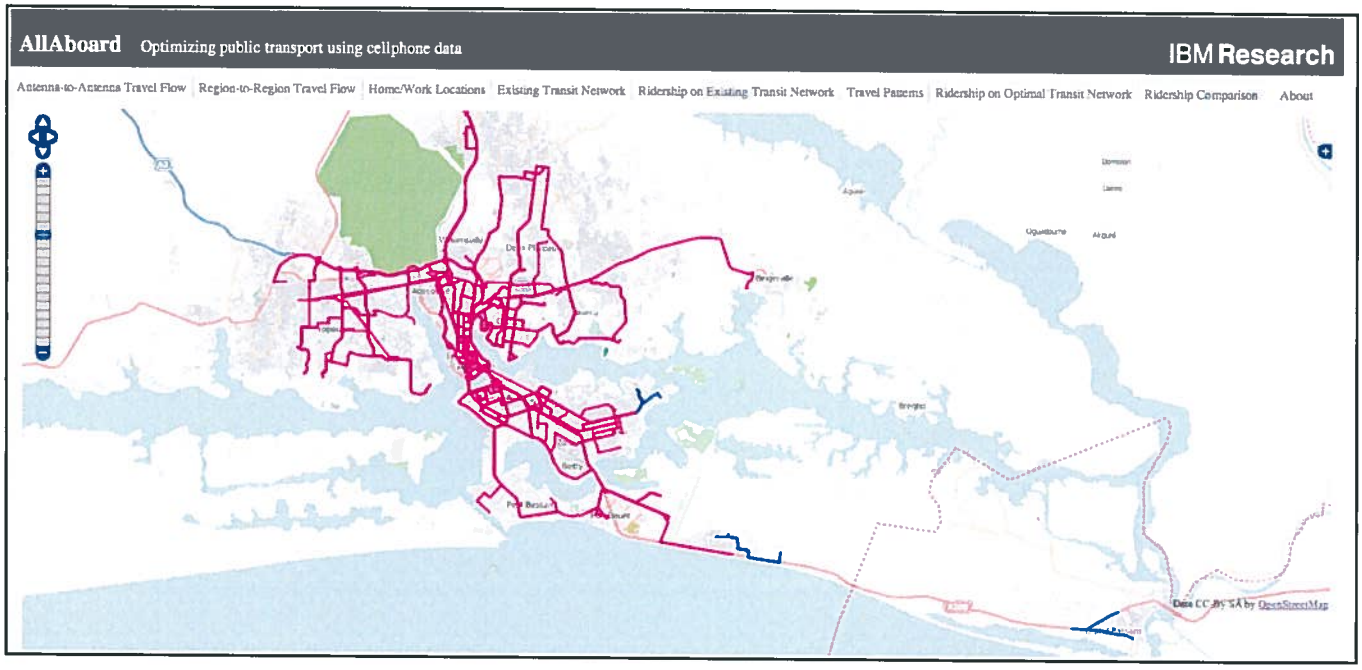


Figure 6: This image shows the existing public transport network (SOTRA) in Abidjan and additional routes suggested by the study. Source: Berlingerio et al., 2013.

By analyzing CDR data, scientists mapped new routes to decongest Abidjan's crowded roads, which would reduce travel time by 10%.

PRIVACY CHALLENGES

There has yet to be a commonly accepted definition of the term "privacy." As defined by OECD, privacy is "an individual's freedom from excessive intrusion in the quest for information and an individual's ability to choose the extent and circumstances under which his or her beliefs, behaviours, opinions and attitudes will be shared with or withheld from others" (OECD, 2005). The majority of risks associated with the misuse of data concern *personal data* or *personally identifiable information*. For this reason, anonymization is common practice when conducting Big Data research.

Robust anonymization of data has been recognized as a critical component of successful research, and academia conforms to strict institutional standards for ethical use of subject data. However, there is increasing awareness regarding the possibility of re-identification of anonymized data. In the Big Data research field, *linkability* refers to the cross-referencing of multiple anonymized data sets, which can be used to recover the identities of people whose data has been anonymized.

It remains true that the safest way to preserve privacy is to irreversibly anonymize and aggregate data sets, but experts continue to explore how to preserve privacy while keeping data sets granular enough to yield valuable insights for public good or social science research.

Several studies have analyzed the exact threshold at which individuals become identifiable. Director of the Harvard University Data Privacy Lab, Dr. Latanya Sweeney, introduced the concept of *k-anonymity*, a way to quantify the order of the risk of personal identification from a data set which decreases in magnitude as the data is made artificially less granular (Sweeney, 2002).

Another recent project used mobility data from 1.5 million mobile phone subscribers in a small Western country, where the location of an individual was specified hourly with a spatial resolution equal to that given by the carrier's antennae in a small Western country, to demonstrate that just four spatio-temporal points were enough to show uniqueness of 95% of the individuals (de Montjoye et al., 2013). By understanding the privacy bounds of human mobility, the data can be 'coarsened,' or made less specific, in order to minimize the chance of personal identification.

Data linkability has also been heavily considered in the health sector. Studying the risks of re-identification, Professor Khaled El Emam offered a system that determines to what degree data sets should be de-identified before release (El Emam, 2010). He suggests the risk can be quantified as a *maximum* level—which is equivalent to the concept of k-anonymity—and quantified as an *average* level, the latter being more appropriate for non-public data releases (El Emam, 2013).

Refraining from sharing one's personal information, even when tightly controlled and in an anonymised or aggregated form, is clearly appealing on an individual level. However, professor and privacy lawyer Jane Yakowitz examines privacy risks versus the value of Big Data for research, and argues that this comes at the greater cost of losing significant policy insights which rely on a large representative sample of data (Yakowitz, 2011).

Ethical guidelines, legal frameworks and technological solutions for protected data sharing are maturing in parallel with the evolution of mobile phone usage around the world and the increased use of Big Data for development and humanitarian purposes. When privacy principles are at the center of the process in any research or technological development, it is referred to as "privacy by design." Proceeding in this way promotes compliance with existing ethical standards by implementing privacy protective mechanisms from the beginning.

PRIVACY BY DESIGN

Privacy by design is a practice that embeds privacy and data protection principles in all research or technological development and across the entire project life cycle.

BIBLIOGRAPHY

DISASTER RESPONSE

Bengtsson L, Xin Lu, Thorson A, Garfield R, von Schreeb J (2011) Improved response to disasters and outbreaks by tracking population movements with mobile phone network data: a post-earthquake geospatial study in Haiti, *PLoS Medicine* 8(8).

Lu X, Bengtsson L, Holme P (2012) Predictability of population displacement after the 2010 Haiti earthquake, *Proceedings of the National Academy of Sciences* 108(29) 11472-11473.

HEALTH

Enrique Frias-Martinez, Graham Williamson and Vanessa Frias-Martinez (2011) An agent-based model of epidemic spread using human mobility and social network information, *3rd International Conference on Social Computing, SocialCom '11*, Boston.

Wesolowski A, Eagle N , Tatem A, Smith D, Noor A, Snow R, Buckee C (2012) Quantifying the impact of human mobility on Malaria, *Science* 338(6104) 267-270.

SOCIO-ECONOMICS

Eagle N, Macy M, Claxton R (2010) Network diversity and economic development, *Science* 328(5981) 1029-1031.

Frias-Martinez V, Virsesa J (2012) On the relationship between socio-economic factors and cell phone usage, *International Conference on Information and Communication Technologies and Development.*

Smith C, Mashadi A, Capra L (2013) Ubiquitous sensing for mapping poverty in developing countries, *Proceedings of the Third Conference on the Analysis of Mobile Phone Datasets.*

TRANSPORTATION

Berlingerio M, Calabrese F, Lorenzo G, Nair R, Pinelli F, Sbodio M (2013) AllAboard: A system for exploring urban mobility and optimizing public transport using cellphone data, *Proceedings of the Third Conference on the Analysis of Mobile Phone Datasets.*

PRIVACY CHALLENGES

OECD (2005) Glossary of Statistical Terms. Retrieved from http://stats.oecd.org/glossary/detail.asp?ID=6959

de Montjoye Y, Hidalgo C, Verleysen M, Blondel V (2013) Unique in the crowd: the privacy bounds of human mobility, *Nature Scientific Reports* (3) 1673. Retrieved from http://www.nature.com/srep/2013/130325/srep01376/full/srep01376.html

Sweeney L (2002) k-Anonymity: a model for protecting privacy, *International Journal of Uncertainty Fuzziness and Knowledge-Based Systems* (10) 557-570.

El Emam K (2010) Risk-based de-identification of health data, *Security & Privacy, IEEE* 8(3) 64,67. doi: 10.1109/MSP.2010.103

El Emam K (2013) Guide to the de-identification of personal health information. CRC Press (Auerbach).

Yakowitz J (2011) Tragedy of the data commons, *Harvard Journal of Law & Technology* (25) 1.

ACKNOWLEDGMENTS

This document has been drafted, edited and produced by the Global Pulse team: Sara Cornish, Olivia De Backer, Anirvan Ghosh, Shehryar Kayani, Robert Kirkpatrick, Jonggun Lee, Tomaz Logar, Miguel Luengo-Oroz, René Clausen Nielsen, Jennifer Poole, Liudmyla Romanoff, Alex Rutherford, Anoush Tatevossian, Makena Walker.

We would like to thank Robert Bond, Khaled El Emam, Kenth Engø-Monsen, Vanessa Frias-Martinez, Yves-Alexandre de Montjoye, Jules Polonetsky and Jane Yakowitz for reviewing drafts and providing feedback on this document.

Contact: info@unglobalpulse.org.

ABOUT GLOBAL PULSE

Global Pulse is an innovation initiative of the United Nations Secretary-General exploring how new, digital data sources and real-time analytics technologies can help policymakers gain a better understanding of changes in human well-being and emerging vulnerabilities. Through strategic public-private partnerships, innovative analysis and open source technology development across its network of Pulse Labs, Global Pulse develops approaches for applying Big Data to 21st century development challenges.

The three-fold implementation strategy includes:

1. **Research & Development:** Conducting research to discover new proxy indicators for tracking development progress and emerging vulnerabilities in real time, and assembling a toolkit of technologies for analyzing real-time data.

2. **Big Data partnerships:** Forging partnerships with companies, organizations, researchers and academic institutions that have the data, technology and analytical expertise needed for Big Data for Development projects and advocacy.

3. **Pulse Lab network:** Establishing an integrated network of country-level innovation centers that bring together government experts, UN agencies, academia and the private sector to prototype and pilot approaches at country level.

For more information please visit www.unglobalpulse.org.

ATTACHMENT 4

Original Investigation

Antidepressant Dose, Age, and the Risk of Deliberate Self-harm

Matthew Miller, MD, ScD; Sonja A. Swanson, ScM; Deborah Azrael, PhD; Virginia Pate, PhD, PhD; Til Stürmer, MD, ScD

Invited Commentary

Supplemental content at jamainternalmedicine.com

IMPORTANCE A comprehensive meta-analysis of randomized trial data suggests that suicidal behavior is twice as likely when children and young adults are randomized to antidepressants compared with when they are randomized to placebo. Drug-related risk was not elevated for adults older than 24 years. To our knowledge, no study to date has examined whether the risk of suicidal behavior is related to antidepressant dose, and if so, whether risk depends on a patient's age.

OBJECTIVE To assess the risk of deliberate self-harm by antidepressant dose, by age group.

DESIGN, SETTING, AND PARTICIPANTS This was a propensity score–matched cohort study using population-based health care utilization data from 162 625 US residents with depression ages 10 to 64 years who initiated antidepressant therapy with selective serotonin reuptake inhibitors at modal or at higher than modal doses from January 1, 1998, through December 31, 2010.

MAIN OUTCOMES AND MEASURES *International Classification of Diseases, Ninth Revision (ICD-9)* external cause of injury codes E950.x-E958.x (deliberate self-harm).

RESULTS The rate of deliberate self-harm among children and adults 24 years of age or younger who initiated high-dose therapy was approximately twice as high as among matched patients initiating modal-dose therapy (hazard ratio [HR], 2.2 [95% CI, 1.6-3.0]), corresponding to approximately 1 additional event for every 150 such patients treated with high-dose (instead of modal-dose) therapy. For adults 25 to 64 years of age, the absolute risk of suicidal behavior was far lower and the effective risk difference null (HR, 1.2 [95% CI, 0.8-1.9]).

CONCLUSIONS AND RELEVANCE Children and young adults initiating therapy with antidepressants at high-therapeutic (rather than modal-therapeutic) doses seem to be at heightened risk of deliberate self-harm. Considered in light of recent meta-analyses concluding that the efficacy of antidepressant therapy for youth seems to be modest, and separate evidence that antidepressant dose is generally unrelated to therapeutic efficacy, our findings offer clinicians an additional incentive to avoid initiating pharmacotherapy at high-therapeutic doses and to closely monitor patients starting antidepressants, especially youth, for several months.

Author Affiliations: Department of Health Policy and Management, Harvard School of Public Health, Boston, Massachusetts (Miller, Azrael), Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts (Swanson), Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill (Pate, Stürmer).

Corresponding Author: Matthew Miller, MD, ScD, Department of Health Policy and Management, Harvard School of Public Health, 677 Huntington Ave, Boston, MA 02115 (mmiller@hsph.harvard.edu).

JAMA Intern Med. doi:10.1001/jamainternmed.2014.1053
Published online April 28, 2014.

The US Food and Drug Administration's (FDA) meta-analysis of antidepressant trials found that children randomized to receive antidepressants had twice the rate of suicidal ideation and behavior compared with children who received placebo.[1] Meta-analysis of adult placebo-controlled trials found that participants 18 to 24 years of age randomized to receive antidepressants were at elevated risk of suicidal thoughts and behavior, those 25 to 64 years of age were at equal risk, and those 65 years or older were at lower risk.[2]

Nonrandomized studies can address some of the limitations of existing randomized antidepressant trials, including their short duration, the small number of suicide-related events observed, the homogeneity of participants, and the different antidepressant types and doses administered across trials. Nonrandomized studies, however, require careful consideration of confounding, especially with respect to the indication for using antidepressants in the first place.[3-8] To minimize such confounding, rigorous observational studies have focused on treatment initiation[9] and avoided nonuser comparison groups.[10,11] In addition, because suicide attempts may lead clinicians to prescribe antidepressants, careful research has eschewed before vs after study designs and instead focused on whether deliberate self-harm (DSH) differs across antidepressant classes and agents. In general, these studies have reported either no evidence of differential risk across class or agent, or small and inconsistent differences.[12-19]

Patients exposed to higher doses of antidepressants tend to experience more frequent and severe adverse effects, including putatively suicidogenic ones, such as akathisia,[20-27] compared with patients prescribed lower doses.[28,29] Despite this dose-related phenomenon and scant evidence that higher doses are more effective in alleviating depressive symptoms,[28,29] neither the FDA meta-analyses nor any observational study to date has examined whether the risk of suicidal behavior is related to antidepressant dose. The current study takes up this question among a cohort of initiators of antidepressant therapy and addresses as well whether dose-related risk is modified by a patient's age.

Methods

Patients and Data Source

The current cohort study involved 162 625 patients 10 to 64 years of age with a depression diagnosis who initiated therapy with selective serotonin reuptake inhibitors (SSRIs) from January 1, 1998, through December 31, 2010. Initiation was defined as filling an SSRI antidepressant prescription without evidence of prescriptions fills for any class of antidepressants in the preceding 12 months. Analyses focus on the first treatment episode. Eligibility required evidence of depression as indicated by an *International Classification of Diseases, Ninth Revision (ICD-9)* code for depression recorded during the 12 months prior to antidepressant initiation (Table 1 and Table 2). To allow uniform assessment and selection of all patients, participants were required to be actively enrolled in a contributing health plan for the 15 months prior to initiation (ie, 12 months for baseline covariate assessment + 2 months [ie, a 60-day grace period] + 30 days [ie, the usual days' supply]). The cohort study was based on observational health care utilization data. Informed consent was not obtained for persons in the data set. The study was exempted by the Harvard School of Public Health institutional review board.

The PharMetrics Claims Database used in this study comprises commercial health plan information obtained from managed care plans throughout the United States. The database includes medical and pharmaceutical claims for over 61 million unique patients from over 98 health plans, and includes *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* inpatient and outpatient diagnoses, Current Procedural Terminology 4 and Healthcare Common Procedure Coding System procedure codes, and both retail and mail-order records of all reimbursed dispensed prescriptions. Our analyses focus on persons younger than 65 years, the age group for which our data are nationally representative of the commercially insured and for which we had sufficient sample size.

Antidepressant Medication Exposure

We restricted analyses to new initiators of therapy with antidepressants, rather than prevalent users, because such a design allows us to detect adverse events that follow soon after therapy with a drug is started, assess risks over time, and control for selection bias with baseline patient characteristics that are not influenced by effects of antidepressant treatment. Incident user designs also mitigate potential bias owing to a patient's drug exposure history influencing current treatment assignment. To further minimize potential confounding by the class of antidepressants prescribed and the use of unusual agents, analyses were restricted to patients initiating therapy with the most commonly prescribed SSRIs (citalopram hydrobromide, sertraline hydrochloride, and fluoxetine hydrochloride), which together constitute 67% of all SSRI therapy initiated.

Patients were assigned to 1 of 3 empirically derived dose categories (modal dose, higher than modal, lower than modal) based on the distribution of doses prescribed among antidepressant initiators. In the 10- to 24-year cohort there were 32 504 in the modal dose category, 7117 in the higher than modal dose category, and 14 542 in the below modal dose category; in the 25- to 64-year-old cohort there were 99 316 in the modal dose category, 23 668 in the higher than modal dose categoy, and 20 065 in the lower than modal dose category. The modal daily dose for citalopram hydrobromide, sertraline hydrochloride, and fluoxetine hydrochloride were, respectively, 20 mg/d, 50 mg/d, and 20 mg/d. Participants who received doses below our empirically derived modal dose often received doses considered below the minimal effective dose for depression[30-32]; to minimize potential confounding, analyses were restricted to participants who received modal dose or doses higher than the modal dose. Patients receiving index doses in excess of the recommended maximum therapeutic dose constituted less than 2% of all patients (112 in the 10- to 24-year-cohort and 677 in the 25- to 64-year-old cohort) and, for similar reasons, were excluded from analysis; maximum daily doses for citalopram hydrobromide, sertraline

Table 1. Baseline Characteristics of the Study Cohort, by Dose, Ages 10 to 24 Years

Baseline Characteristic[a]	Cohort, No. (%)			
	Prematched[b]		Propensity Score-Matched	
	Modal Dose (n = 32 504)	High Dose (n = 7117)	Modal Dose (n = 13 948)	High Dose (n = 7108)
Age, y				
10-15	6346 (19.5)	1423 (20.0)	2964 (21.3)	1421 (20.0)
16-19	14 995 (46.1)	3182 (44.7)	6104 (43.8)	3179 (44.7)
20-24	11 163 (34.3)	2512 (35.3)	4880 (35.0)	2508 (35.3)
Male sex	10 949 (33.7)	2704 (38.0)	5054 (36.2)	2698 (38.0)
Severity level of depression diagnosis[c]				
Tier 1: Primary inpatient diagnosis ≤30 d preindex	1296 (4.0)	315 (4.4)	601 (4.3)	315 (4.4)
Tier 2: Primary inpatient diagnosis31-360 d preindex	202 (0.6)	74 (1.0)	128 (0.9)	72 (1.0)
Tier 3: Nonprimary inpatient diagnosis ≤360 d preindex	616 (1.9)	194 (2.7)	364 (2.6)	191 (2.7)
Tier 4: ≥2 Outpatient diagnoses ≤360 d preindex	17 707 (54.5)	4425 (62.2)	8670 (62.2)	4421 (62.2)
Tier 5: 1 Inpatient diagnosis≤360 d preindex	12 683 (39.0)	2109 (29.6)	4185 (30.0)	2109 (29.7)
Anxiety disorders	6808 (20.9)	1841 (25.9)	3501 (25.1)	1836 (25.8)
Deliberate self-harm	451 (1.4)	106 (1.5)	183 (1.3)	104 (1.5)
Primary inpatient depression diagnosis	1498 (4.6)	389 (5.5)	729 (5.2)	387 (5.4)
No depression diagnosis within 30 d of index date	3892 (12.0)	1327 (18.6)	2389 (17.1)	1318 (18.5)
Suicidal ideation ≤30 d prior to anxiety disorder initiation (2006 forward only)	522 (2.6)	113 (2.9)	254 (3.1)	113 (2.9)
Attention-deficit/hyperactivity disorder	3218 (9.9)	856 (12.0)	1577 (11.3)	854 (12)
Cognitive impairment or dementia	10 (0.0)	3 (0.0)	6 (0.0)	3 (0.0)
Personality disorder	288 (0.9)	74 (1.0)	145 (1.0)	74 (1.0)
Substance abuse	2787 (8.6)	655 (9.2)	1243 (8.9)	652 (9.2)
Use of any opiate	7239 (22.3)	1486 (20.9)	2908 (20.8)	1484 (20.9)
Distinct drug prescriptions filled, No.				
1 (antidepressant only)	5082 (15.6)	1349 (19.0)	2557 (18.3)	1346 (18.9)
2-3	9967 (30.7)	2229 (31.3)	4428 (31.7)	2226 (31.3)
4-5	7379 (22.7)	1546 (21.7)	3056 (21.9)	1546 (21.8)
6-9	7212 (22.2)	1400 (19.7)	2763 (19.8)	1399 (19.7)
≥10	2864 (8.8)	593 (8.3)	1144 (8.2)	591 (8.3)
≥1 Psychiatric hospitalizations	1554 (4.8)	418 (5.9)	774 (5.5)	413 (5.8)
Outpatient visits, No.				
0-4	7308 (22.5)	1447 (20.3)	2818 (20.2)	1447 (20.4)
5-9	9635 (29.6)	2021 (28.4)	4010 (28.7)	2021 (28.4)
10-19	9904 (30.5)	2236 (31.4)	4461 (32.0)	2235 (31.4)
20-39	4715 (14.5)	1134 (15.9)	2165 (15.5)	1132 (15.9)
≥40	942 (2.9)	279 (3.9)	494 (3.5)	273 (3.8)
Hospitalizations				
≥1 for substance abuse	205 (0.6)	59 (0.8)	114 (0.8)	59 (0.8)
≥1 for other reasons	2148 (6.6)	468 (6.6)	922 (6.6)	467 (6.6)
Cancer				
Lung	2 (0.0)	2 (0.0)	2 (0.0)	2 (0.0)
Colorectal	3 (0.0)	0	0	0
Other malignant neoplasm	153 (0.5)	45 (0.6)	80 (0.6)	45 (0.6)
Cardiac arrhythmias	554 (1.7)	148 (2.1)	261 (1.9)	148 (2.1)
Congestive heart failure	20 (0.1)	5 (0.1)	10 (0.1)	5 (0.1)
Arthritis	70 (0.2)	8 (0.1)	16 (0.1)	8 (0.1)
Cerebrovascular disease	72 (0.2)	19 (0.3)	37 (0.3)	19 (0.3)
Cluster headaches or migraines	1168 (3.6)	237 (3.3)	469 (3.4)	236 (3.3)
Diabetes mellitus	386 (1.2)	91 (1.3)	173 (1.2)	90 (1.3)
Disorders of the eye	17 (0.1)	1 (0.0)	2 (0.0)	1 (0.0)

(continued)

Table 1. Baseline Characteristics of the Study Cohort, by Dose, Ages 10 to 24 Years (continued)

Baseline Characteristic[a]	Cohort, No. (%)			
	Prematched[b]		Propensity Score–Matched	
	Modal Dose (n = 32 504)	High Dose (n = 7117)	Modal Dose (n = 13 948)	High Dose (n = 7108)
Gait or balance disorder	108 (0.3)	18 (0.3)	37 (0.3)	18 (0.3)
Postural hypotension	57 (0.2)	22 (0.3)	40 (0.3)	22 (0.3)
Hyperparathyroidism	5 (0.0)	0	0	0
Osteoarthritis	112 (0.3)	37 (0.5)	64 (0.5)	35 (0.5)
Osteoporosis	12 (0.0)	5 (0.1)	8 (0.1)	4 (0.1)
Parkinson disease	1	0	0	0
Seizures	216 (0.7)	63 (0.9)	118 (0.8)	61 (0.9)
Urinary incontinence	163 (0.5)	36 (0.5)	73 (0.5)	35 (0.5)
Physician prescriber type				
General practitioner or internist	14 430 (44.4)	2358 (33.1)	4694 (33.7)	2358 (33.2)
Psychiatrist	6735 (20.7)	2108 (29.6)	3970 (28.5)	2101 (29.6)
Other	11 339 (34.9)	2651 (37.3)	5284 (37.8)	2649 (37.2)
SSRI				
Citalopram hydrobromide	9500 (29.2)	1586 (22.3)	3238 (23.2)	1586 (22.3)
Fluoxetine hydrochloride	11 005 (33.9)	1203 (16.9)	2307 (16.5)	1203 (16.9)
Sertraline hydrochloride	11 999 (36.9)	4328 (60.8)	8403 (60.2)	4319 (60.8)

Abbreviation: SSRI, selective serotonin reuptake inhibitor.

[a] For our younger-aged cohorts, the strongest predictors of initiating therapy with high- rather than modal-dose antidepressants (when all factors in Table 1 and Table 2 are simultaneously adjusted) include having been admitted to a psychiatric hospital in the year prior to starting antidepressant therapy, having an internist (rather than a psychiatrist or other health professional) prescribe the initial antidepressant, taking no prescription medications other than the antidepressant initiated, and being prescribed sertraline rather than either fluoxetine or citalopram (see eTable 1 and eTable 2 in Supplement).

[b] From January 1, 1998, through December 31, 2010, 624 171 patients initiated therapy with 1 of the study antidepressants, 607 538 initiated monotherapy. Of the 222 896 patients with baseline depression and no prior antidepressant use in the washout period, 202 605 were 10 to 64 years of age. Of these, 167 092 initiated therapy at or above the modal dose (166 253 within the therapeutic range (ie, excluding patients with subtherapeutic doses), and 162 605 did so without baseline bipolar disorder or schizophrenia (162 605 within the therapeutic range).

[c] *International Classification of Diseases, Ninth Revision* codes 296.2x, 296.3x, 298.0x, 300.4x, 309.0x, 309.1x, 311.xx, 293.83, 296.90, 309.28.

hydrochloride, and fluoxetine hydrochloride were, respectively, 40 mg/d, 200 mg/d, and 80 mg/d. Patients initiating therapy with more than 1 drug or with more than 1 dosing regimen were also excluded from analyses.

Follow-up and Study End Point

Exposure status was assigned based on the initiated medication. Study follow-up began on the day after initiation of the first antidepressant therapy. When a dispensing occurred before the previous prescription should have run out, use of the new prescription was assumed to have begun the day after the end of the old prescription. Primary analyses used a 60-day grace period (≤60 days beyond the provided days' supply can elapse before censoring).

Patients were censored the date they switched agents, added other antidepressant agents, changed dose, 360 days after the index date, ended enrollment in their health insurance plan, engaged in DSH, or the end of the study period, whichever came first.

The first occurrence of DSH was our outcome of interest, and it was defined as a medical claim with an *ICD-9* external cause of injury code (e-code) (E950.x-E958.x).

Patient Characteristics

Baseline patient characteristics included age, sex, medical comorbidities, treatment history, and concomitant medication use in the 12 months prior to initiation of antidepressant therapy. Psychiatric risk factors included the number of acute psychiatric hospitalizations, the number of acute hospitalizations for substance abuse, psychiatric comorbidity, and prior DSH. A hierarchy of depression was constructed as a function of the proximity of the most recent depression diagnosis to antidepressant initiation and whether the diagnosis was rendered during an inpatient stay or an outpatient visit.

Statistical Analysis

Patients were divided into 2 age groups guided by the age-related risk of suicidal behavior identified in the FDA's meta-analyses (ages 10-24 years vs 25-64 years). We estimated propensity scores for treatment initiation of high vs modal dose for each age group separately based on the patient characteristics described in the previous subsection (age is modeled as a continuous variable within each cohort). Up to 2 patients receiving a modal dose were matched to every patient receiving a high dose using an adaptation of a published propensity score algorithm.[33] Thus, the research question we addressed is what would have happened, with respect to future DSH, if people who initiated high-dose therapy had instead initiated with modal-dose therapy.

Crude rates of DSH were calculated over the 1-year exposure period (ie, subject to censoring as described herein). Crude rates were also reported for 3 time periods after initiating

Table 2. Baseline Characteristics of the Study Cohort, by Dose, Ages 25 to 64 Years

Baseline Characteristic[a]	Cohort, No. (%)			
	Prematched[b]		Propensity Score-Matched	
	Modal Dose (n = 99 316)	High Dose (n = 23 668)	Modal Dose (n = 45 002)	High Dose (n = 23 637)
Age, y				
25-40	42 808 (43.1)	9622 (40.7)	18 619 (41.4)	9618 (40.7)
41-55	41 538 (41.8)	10 156 (42.9)	19 260 (42.8)	10 143 (42.9)
≥56	14 970 (15.1)	3890 (16.4)	7123 (15.8)	3876 (16.4)
Male sex	32 547 (32.8)	8381 (35.4)	15 672 (34.8)	8365 (35.4)
Severity level of depression diagnosis[c]				
Tier 1: Primary inpatient diagnosis ≤30 d preindex	836 (0.8)	321 (1.4)	563 (1.3)	321 (1.4)
Tier 2: Primary inpatient diagnosis 31-360 d preindex	126 (0.1)	80 (0.3)	102 (0.2)	77 (0.3)
Tier 3: Nonprimary inpatient diagnosis ≤360 d preindex	2105 (2.1)	736 (3.1)	1290 (2.9)	735 (3.1)
Tier 4: ≥2 Outpatient diagnoses ≤360 d preindex	48 237 (48.6)	13 610 (57.5)	25 532 (56.7)	13 585 (57.5)
Tier 5: 1 Outpatient diagnosis ≤360 d preindex	48 012 (48.3)	8921 (37.7)	17 515 (38.9)	8919 (37.7)
Anxiety disorders	20 844 (21.0)	5731 (24.2)	10 764 (23.9)	5719 (24.2)
Deliberate self-harm	217 (0.2)	68 (0.3)	119 (0.3)	68 (0.3)
Primary inpatient depression diagnosis	962 (1.0)	401 (1.7)	665 (1.5)	398 (1.7)
No depression diagnosis within 30 d of index date	15 710 (15.8)	6680 (28.2)	11 499 (25.6)	6649 (28.1)
Suicidal ideation ≤30 d prior to anxiety disorder initiation (2006 forward only)	406 (0.6)	115 (0.8)	244 (0.9)	115 (0.8)
Cognitive impairment or dementia	70 (0.1)	30 (0.1)	43 (0.1)	29 (0.1)
Personality disorder	462 (0.5)	184 (0.8)	299 (0.7)	178 (0.8)
Substance abuse	8853 (8.9)	2343 (9.9)	4265 (9.5)	2336 (9.9)
Use of any opiate	32 512 (32.7)	7422 (31.4)	14 469 (32.2)	7417 (31.4)
Distinct drug prescriptions filled, No.				
1 (antidepressant only)	9018 (9.1)	2892 (12.2)	5096 (11.3)	2877 (12.2)
2-3	23 047 (23.2)	5972 (25.2)	10 963 (24.4)	5963 (25.2)
4-5	20 807 (21.0)	4676 (19.8)	9117 (20.3)	4671 (19.8)
6-9	26 773 (27.0)	5828 (24.6)	11 395 (25.3)	5826 (24.6)
≥10	19 671 (19.8)	4300 (18.2)	8431 (18.7)	4300 (18.2)
≥ 1 Psychiatric hospitalizations	1025 (1.0)	419 (1.8)	698 (1.6)	416 (1.8)
Outpatient visits, No.				
0-4	18 846 (19.0)	4217 (17.8)	8087 (18.0)	4213 (17.8)
5-9	24 715 (24.9)	5479 (23.1)	10 549 (23.4)	5477 (23.2)
10-19	29 477 (29.7)	6890 (29.1)	13 130 (29.2)	6885 (29.1)
20-39	19 340 (19.5)	4982 (21.0)	9378 (20.8)	4971 (21.0)
≥40	6938 (7.0)	2100 (8.9)	3858 (8.6)	2091 (8.8)
Hospitalizations, No.				
≥ 1 for substance abuse	483 (0.5)	165 (0.7)	300 (0.7)	165 (0.7)
≥ 1 for other reasons	11 034 (11.1)	2720 (11.5)	5171 (11.5)	2716 (11.5)
Cancer				
Lung	203 (0.2)	50 (0.2)	96 (0.2)	50 (0.2)
Breast	125 (0.1)	25 (0.1)	46 (0.1)	25 (0.1)
Colorectal	218 (0.2)	53 (0.2)	103 (0.2)	53 (0.2)
Prostate	272 (0.3)	62 (0.3)	126 (0.3)	62 (0.3)
Other malignant neoplasm	3155 (3.2)	803 (3.4)	1485 (3.3)	799 (3.4)
Attention-deficit/hyperactivity disorder	1259 (1.3)	474 (2.0)	781 (1.7)	467 (2.0)
Cardiac arrhythmias	3591 (3.6)	946 (4.0)	1760 (3.9)	944 (4.0)
Congestive heart failure	962 (1.0)	311 (1.3)	531 (1.2)	311 (1.3)
Arthritis	856 (0.9)	250 (1.1)	462 (1.0)	248 (1.0)
Cerebrovascular disease	1859 (1.9)	525 (2.2)	953 (2.1)	524 (2.2)
Diabetes mellitus	7514 (7.6)	2077 (8.5)	3640 (8.1)	1997 (8.5)

(continued)

Table 2. Baseline Characteristics of the Study Cohort, by Dose, Ages 25 to 64 Years (continued)

Baseline Characteristic[a]	Cohort, No. (%)			
	Prematched[b]		Propensity Score–Matched	
	Modal Dose (n = 99 316)	High Dose (n = 23 668)	Modal Dose (n = 45 002)	High Dose (n = 23 637)
Cluster headaches or migraines	4283 (4.3)	1164 (4.9)	2117 (4.7)	1161 (4.9)
Disorders of the eye	117 (0.1)	29 (0.1)	57 (0.1)	29 (0.1)
Gait or balance disorder	964 (1.0)	291 (1.2)	501 (1.1)	290 (1.2)
Postural hypotension	184 (0.2)	47 (0.2)	87 (0.2)	46 (0.2)
Hyperparathyroidism	141 (0.1)	34 (0.1)	70 (0.2)	34 (0.1)
Osteoarthritis	6004 (6.0)	1695 (7.2)	3034 (6.7)	1689 (7.1)
Osteoporosis	1479 (1.5)	365 (1.5)	689 (1.5)	365 (1.5)
Parkinson disease	94 (0.1)	17 (0.1)	36 (0.1)	17 (0.1)
Seizures	650 (0.7)	211 (0.9)	365 (0.8)	210 (0.9)
Urinary incontinence	1002 (1.0)	300 (1.3)	562 (1.2)	299 (1.3)
Physician prescriber type				
General practitioner or internist	59 059 (59.5)	11 501 (48.6)	22 791 (50.6)	11 500 (48.7)
Psychiatrist	11 012 (11.1)	4902 (20.7)	8132 (18.1)	4872 (20.6)
Other	29245 (29.4)	7265 (30.7)	14079 (31.3)	7265 (30.7)
SSRI				
Citalopram hydrobromide	37 172 (37.4)	6465 (27.3)	13 063 (29.0)	6465 (27.4)
Fluoxetine hydrochloride	27 061 (27.2)	3742 (15.8)	6834 (15.2)	3742 (15.8)
Sertraline hydrochloride	35 083 (35.3)	13 461 (56.9)	25 105 (55.8)	13 430 (56.8)

Abbreviation. SSRI, selective serotonin reuptake inhibitor.

[a] For the older-aged cohorts, the strongest predictors of being initiated with high- rather than modal-dose antidepressants include having an internist (rather than a psychiatrist or other health professional) prescribe the initial antidepressant, not taking prescription medications other than the antidepressant initiated, and being prescribed sertraline rather than either fluoxetine or citalopram (see eTable 2 in Supplement).

[b] From January 1, 1998, through December 31, 2010, 624 171 patients initiated therapy with 1 of the study antidepressants, 607 538 initiated monotherapy. Of the 222 896 patients with baseline depression and no prior antidepressant use in the washout period, 202 605 were 10 to 64 years of age. Of these, 167 092 initiated therapy at or above the modal dose (166 253 within the therapeutic range (ie, excluding patients with subtherapeutic doses), and 162 605 did so without baseline bipolar disorder or schizophrenia (162 605 within the therapeutic range).

[c] *International Classification of Diseases, Ninth Revision* (codes 296.2x, 296.3x, 298.0x, 300.4x, 309.0x, 309.1x, 311.xx, 293.83, 296.90, 309.28.

therapy: days 1 to 30, days 31-90, and days 91-360. Exact methods were used to calculate 95% confidence intervals. Modified Poisson regression using an identity link was used to estimate the 90-day risk differences; Cox models were used to estimate hazard ratios (HRs).

Sensitivity analyses examined how robust our findings were to a range of grace periods. Additional subgroup analyses restricted participants to those without a prior suicide attempt and to those who had not received antidepressants in the 3 years prior to their index date. In mid-2005 a new diagnostic billing code for suicidal ideation became available. We used this historical development to assess the extent to which our primary analyses may have been confounded by this well-established predictor of DSH by examining the extent to which matched cohorts based on propensity score algorithms that did not incorporate suicidal ideation achieved balance on suicidal ideation and the extent to which adjusting for suicidal ideation as a covariate in Cox models attenuated the risk of suicide attempts associated with higher dose.

Bias analyses assessed the strength of residual confounding that would need to be present to fully explain associations found in our primary analyses.[34,35] Specifically, we estimated the strength of a single dichotomous unmeasured confounder that would be necessary to nullify the estimated 90-day risk difference. Bias in the risk difference is dependent on 2 factors: how predictive the hypothetical confounder is of attempts, and how imbalanced the confounder is across high- vs modal-dose treatment groups (both assessed on the additive scale). A priori, we expected depression severity (eg, prior inpatient stays or psychiatric comorbidities) and a history of suicidality (eg, prior ideation or attempts) to be the strongest potential confounders. Accordingly, we present the magnitude of confounding introduced by these measured confounders in the prematched cohort along with the bias analyses.

Results

Baseline patient characteristics in age-group-stratified, propensity score-matched cohorts of high- vs modal-dose users were well balanced across dose categories (Table 1 and Table 2). For example, the age and sex distributions among high- vs modal-dose initiators were almost identical, and the distribution of our constructed tiers of depression severity differed little across dose categories. Suicidal ideation was also closely balanced across dose cohorts within each age stratum even though it did not contribute to the matching algorithm. Approximately half of all patients (45%) with a depression diagnosis

Table 3. Rate of Deliberate Self-harm (DSH)[a] per 1000 Person-years, by Dose and Age Group Over the First Year After Initiating Therapy, and by Time Since Initiating Therapy

Dose	Patients Initiating Therapy, No.	DSH Events	Person-years ×1000	DSH Rate (per 1000 Person-years)	DSH Rate (95% CI) by Time Since Index Date (No. of Events), d		
					0-30	31-90	91-360
Age 10-24 y							
High	7116	74	2 351.10	31.5 (24.9-39.3)	51.8 (35.4-73.4) (n = 29 patients)	36.8 (25.6-51.2) (n = 32 patients)	14.1 (7.9-23.4) (n = 13 patients)
Modal	14 189	68	4 628.50	14.7 (11.5-18.5)	20.9 (13.6-30.8) (n = 23 patients)	19.0 (13.3-26.4) (n = 33 patients)	6.7 (3.7-11.3) (n = 12 patients)
Age 25-64 y							
High	23 637	32	9 855.74	3.2 (2.3-4.5)	4.2 (2.0-8.0) (n = 8 patients)	2.8 (1.4-5.2) (n = 9 patients)	3.1 (1.8-5.0) (n = 15 patients)
Modal	45 002	49	17 672.36	2.8 (2.1-3.6)	7.5 (5.1-10.8) (n = 27 patients)	2.2 (1.2-3.6) (n = 13 patients)	1.1 (0.5-2.0) (n = 9 patients)

[a] Acts of self-harm of undetermined intent are not included in analyses (and constitute 19% of self-harm events that occurred during treatment among antidepressant initiators in our cohort). Most DSH claims in our analyses (88%) resulted from visits to emergency departments or hospital admissions.

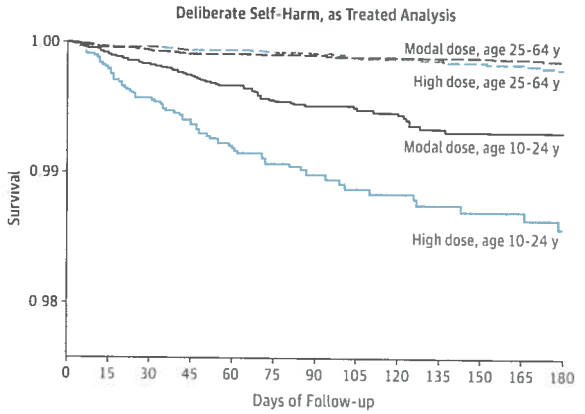
who initiated high-dose SSRIs therapy (30 785) filled prescriptions written by internists or general practitioners (13 859) (Table 1 and Table 2). Among patients younger than 25 years, internists and/or general practitioners wrote one-third (33%) of all initial high-dose prescriptions; psychiatrists and/or psychologists wrote 30% of all such prescriptions (Table 1). Among patients 25 to 64 years of age, internists and/or general practitioners wrote 49% of all such high-dose prescriptions; psychiatrists and/or psychologists wrote 21% of such prescriptions (Table 2). Roughly one-third (32%) of all high-dose antidepressant initiators received prescription written by other types of physicians (31% among patients aged 25 to 64 years [Table 2], 37% among patients aged ≤24 years [Table 1]; 10% of the latter physicians were pediatricians [data not shown]).

In our matched cohorts, 142 participants ages 10 to 24 years (68 modal-dose initiators, 74 high-dose initiators) engaged in DSH within 1 year of treatment initiation; the corresponding rates of DSH for the modal- vs high-dose initiators were 14.7 (95% CI, 11.5-18.5) and 31.5 (95% CI, 24.9-39.3) events per 1000 person-years, respectively. For participants ages 25 to 64 years, there were 81 such acts (49 in modal-dose initiators, 32 in high-dose initiators), corresponding to rates of 2.8 (95% CI, 2.1-3.6) and 3.2 (95% CI, 2.3-4.5) events per 1000 person-years for the modal- vs high-dose participants, respectively (Table 3). Although the hazards were proportional throughout the 1-year follow-up period, most of the events occurred in the first 3 months after initiation (Table 3, Figure 1).

Propensity score–matched analyses produced HRs that were substantially higher in the 10- to 24-year-old cohorts than in the older cohorts (Table 4): among 10- to 24-year-olds the rate of DSH among high-dose participants was approximately double that among modal-dose participants (HR, 2.2; 95% CI, 1.6-3.0); for participants 25 to 64 years of age, the HR was considerably lower (HR, 1.2; 95% CI, 0.8-1.9). The age group by dose interaction achieved statistical significance ($P = .04$) (data not shown).

Findings for the young cohort were robust to several different model specifications, including analyses that varied the grace period from 7 to 360 days, excluded participants without a DSH history prior to their index prescription. and among patients who were treatment naïve for at least 3 years (Table 4). The DSH HRs for high vs modal dose among those initiating

Figure 1. Probability of Remaining Free of Deliberate Self-harm and Time Since Initiating High- vs Modal-Dose Antidepressant Therapy, by Age Group



therapy in 2006 or later were found to be consistent with those found for the entire study period. Moreover, DSH HRs among this population were virtually identical regardless of whether Cox models adjusted for suicidal ideation (because suicidal ideation, while strongly predictive of the outcome, was not strongly related to dose) (Table 4).

In our primary analysis of the 10- to 24-year-old cohort, for every 1000 patients initiating high-dose therapy there were approximately 7 (7.3) more DSH events over the first 90 days of treatment among high-dose initiators compared with modal-dose initiators (95% CI, 3.6-11.1) (Table 4). The corresponding number needed to harm was 136. For the older cohort, the risk difference was effectively zero. Not all acts of DSH are e-coded in claims data (eg, some overdose by drug events are known to occur but lack e-codes, leading to underestimates of both intentional and unintentional overdose event rates). Although this is likely to be nondifferential with respect to our exposure of interest and therefore is unlikely to bias estimates appreciably because event rates are underestimated, the number needed to harm we derived is likely a conservative estimate (ie, an upper bound on the true number needed to harm).

Table 4. Deliberate Self-harm (DSH) Comparing Propensity Score–Matched Participants Initiating High-Dose vs Modal-Dose Antidepressant Therapy[a]

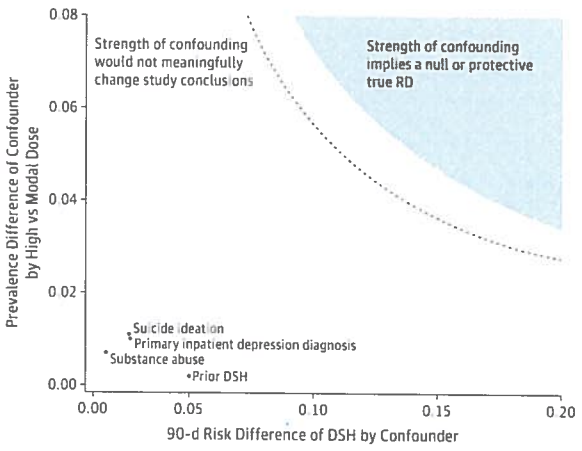
Analysis	1-Year HR (95% CI)	90-d Risk Difference per 1000 Persons (95% CI)	No. Needed to Harm
10- to 24-Year-Old Cohort			
Duration of grace period, d			
60[b]	2.2 (1.6 to 3.0)	7.3 (3.6 to 11.1)	136.2
7	2.1 (1.4 to 3.2)	18.2 (7.2 to 29.1)	55.0
14	2.0 (1.4 to 3.0)	15.8 (6.7 to 24.9)	63.2
30	2.3 (1.6 to 3.2)	12.7 (6.7 to 18.8)	78.4
90	2.1 (1.5 to 2.8)	6.9 (3.3 to 10.5)	145.0
180	2.0 (1.5 to 2.7)	6.9 (3.3 to 10.5)	145.0
360	1.7 (1.3 to 2.2)	6.9 (3.3 to 10.5)	145.0
First treatment carried forward	1.4 (1.1 to 1.8)	5.8 (2.9 to 8.7)	171.8
No history of baseline DSH	2.1 (1.5 to 3.0)	7.3 (3.7 to 10.9)	137.4
3-y treatment naive	1.7 (1.0 to 2.8)	6.5 (0.1 to 12.8)	154.8
2006-2010 data only: no SI adjustment	1.8 (1.2 to 2.6)	8.4 (2.8 to 14.1)	118.5
2006-2010 data only: adjusting for SI	1.8 (1.2 to 2.6)	8.9 (3.3 to 14.5)	112.6
25- to 64-Year-Old Cohort			
Duration of grace period, d			
60[b]	1.2 (0.8 to 1.9)	−0.2 (−0.8 to 0.4)	NS
7	1.0 (0.6 to 1.8)	−0.3 (−1.7 to 1.1)	NS
14	0.9 (0.5 to 1.5)	−0.6 (−1.9 to 0.6)	NS
30	1.0 (0.6 to 1.7)	−0.6 (−1.4 to 0.3)	NS
90	1.2 (0.8 to 1.9)	−0.2 (−0.8 to 0.3)	NS
180	1.3 (0.9 to 2.0)	−0.2 (−0.8 to 0.3)	NS
360	1.4 (0.9 to 2.0)	−0.2 (−0.8 to 0.3)	NS
First treatment carried forward	1.4 (1.0 to 1.9)	−0.1 (−0.7 to 0.5)	NS
No history of baseline DSH	1.1 (0.7 to 1.8)	−0.3 (−0.9 to 0.3)	NS
3-y treatment naive	2.1 (0.9 to 4.8)	0.7 (−0.4 to 1.7)	NS
2006-2010 data only: no SI adjustment	1.3 (0.8 to 2.3)	−0.1 (−1.0 to 0.7)	NS
2006-2010 data only: adjusting for suicidal ideation	1.3 (0.8 to 2.2)	−0.0 (−0.9 to 0.8)	NS

Abbreviations: DSH, deliberate self-harm; NS, not significant clinically or statistically; SI, suicidal ideation.

[a] Hazard ratios (HRs) for deliberate self-harm (DSH) during 1-year of follow-up comparing propensity score–matched participants initiating high-dose vs modal-dose antidepressant therapy, risk differences per 1000 persons over the first 90 days of therapy, and corresponding number of patients needed to be treated to result in 1 additional suicide attempt

[b] Primary analysis. Sensitivity analyses of our unmatched cohort produced HRs similar to those from our (propensity score) matched analyses, not only when models adjusted for (ie, included a covariate for) the propensity to be treated with high-dose therapy, but also in crude and age- and sex-adjusted models. For example, crude, age- and sex-adjusted, and propensity score–adjusted HRs (95% CIs) of our unmatched 10- to 24-year-old cohorts were, respectively, 1.72 (95% CI, 1.32-2.25), 1.77 (95% CI, 1.36-2.32), and 1.87 (95% CI, 1.42-2.46) (not shown).

Figure 2. Bias Analysis for 10- to 24-Year-Old Cohort



DSH indicates deliberate self-harm, RD, risk difference. The dotted line indicates the strength of confounding implied if true RD is 2 attempts per 1000. The shaded area indicates the strength of confounding implied if the true risk difference is null or protective.

Figure 2 depicts how strong a risk factor and how imbalanced a hypothetical unmeasured confounder would need to be in order to nullify our 90-day risk difference in the younger cohort. As can be seen, a putative confounder that would nullify our findings (or even reduce the risk difference to what we considered a clinically meaningful difference of 2 events per 1000 patients) would need to be both far more predictive of subsequent DSH than our most highly predictive covariates (history of DSH, suicidal ideation, substance abuse, or inpatient hospitalization for depression) and also an order of magnitude more imbalanced across dose levels than our most imbalanced prematched covariate. It is important to note that such an unmeasured confounder would need to be this strong in the *matched* cohort; that is, it would need to be very strongly associated with dose and subsequent DSH even after adjustment for all the measured confounders accounted for in the propensity score–matching process.

Discussion

To our knowledge, the current investigation is the first prospective cohort study to examine the relation between dose

of antidepressants and the risk of DSH. We found that the rate of DSH for children and young adults was approximately twice as large among patients initiating high-dose therapy compared with those initiating modal-dose therapy. Given the high baseline rates of DSH among these patients, we expect approximately 1 additional DSH event for every 136 patients 10 to 24 years of age who are treated with high-dose therapy (instead of modal-dose therapy). For the older cohorts, the absolute risk of DSH was far lower, and the difference in risk between the cohorts was effectively null.

Several possible mechanisms linking antidepressant use to suicidal behavior have been suggested,[20,23-26,36-39] including an early energizing effect that allows patients with depression to act on suicidal impulses, suicidogenic adverse effects (eg, akathisia, insomnia, panic attacks), episode-shifting effects (from depressive to manic episodes), and paradoxical worsening of depression. Although our study does not address the mechanisms whereby higher doses might lead to higher suicide risk, if depression-independent suicidogenic effects increase with dose, as has been observed for akathesia,[28] but antidepressive effects are insensitive to doses within a broad therapeutic range, as seems to be the case,[29,40-45] higher doses might produce a net tendency toward suicidal behavior.

To the extent that depression-independent suicidogenic effects of antidepressants exist, older adults may be less susceptible, on balance, if the antidepressive efficacy of antidepressants is superior for older adults compared with children and younger adults.[46,47] Our finding that dose-related suicide risk seems to be more pronounced among children and young adults might also reflect an age-related susceptibility to suicidogenic effects of antidepressants independent of depression severity, as was observed in randomized trials with placebo controls.[1]

The elevated risk of DSH we observe among youth receiving therapy with high-dose antidepressants compared with those receiving therapy with a modal dose might also be due to more frequent and severe drug discontinuation syndromes among patients receiving high-dose therapy.[48] Although we censor at known discontinuation of therapy, it is still possible that differential nonadherence and/or differential severity of withdrawal reactions due to nonadherence contributed to our findings. This form of nondifferential adherence would, however, bias findings to the null, as would poorer adherence that was related to untoward adverse effects, which in general tend to be more common among high-dose users, suggesting that our estimate of the risk of DSH associated with high-dose therapy is conservative. The robustness of our findings to grace periods as disparate as 1 week to 1 year also militates against withdrawal reactions playing a major role. Finally, the half-lives of our SSRIs are relatively long (range, 16-35 hours),[49] making severe withdrawal reactions less likely.

To examine the extent to which confounding not explicitly modeled in our propensity score adjustment may account for our results, we applied our primary matching algorithm, which did not include a covariate for baseline suicidal ideation, to data from 2006 through 2010. Baseline suicidal ideation, while a potent predictor of subsequent DSH (as expected), was not associated with dose (even across unmatched cohorts), suggesting that other potential but unaccounted-for risk factors for DSH might also be reasonably balanced across our cohorts defined by dose. Although it is still possible that unmeasured confounding accounts for the dose-response relationship we observed, it is not obvious what other factors might have led to meaningful confounding of our results. Indeed, such an unmeasured confounder would have to possess a very strong association with both dose and suicidal behavior—and also remain largely uncorrelated with risk factors we explicitly accounted for in analyses. Estimates from our bias analysis suggest that any such unmeasured confounder would need to be both more predictive of subsequent DSH than the most highly predictive risk factor in our data set (history of DSH) and also an order of magnitude more imbalanced across dose levels than our most imbalanced covariate.

When interpreting findings from the current study, one should bear in mind several additional caveats. First, as in all analyses relying on claims databases, we have limited ability to adjust for the severity of psychiatric illness. We do, however, use propensity score techniques to adjust for psychiatric comorbidity and comedication and for a proxy of depression severity involving whether a patient's depression diagnosis occurred during an inpatient admission for depression, whether the diagnosis was a primary or secondary diagnosis, and whether the diagnosis occurred within the month prior to their index date or more remotely. Propensity scores offer an advantage in studies of rare outcomes (eg, DSH) because propensity scores model the relation of covariates and their interactions with the drug exposure (which is relatively frequent) and not directly with the study outcome (which is often rare), thereby mitigating the risk of overfitting in a traditional outcome model.[50,51] As is the case for all observational studies, however, our ability to adjust fully for underlying suicide risk at baseline depends on our ability to accurately classify baseline confounders—and is compromised to the extent that measurement and reporting of conditions coded on insurance claims are misclassified.[52] Second, we used administrative data and therefore did not measure antidepressant adherence directly. Using automated prescription data may, however, more accurately measure use than studies that rely on data from self-report surveys.[53-55] A related point is that we define drug exposure in our primary analysis in a way that seeks to capture how patients fill their medications (ie, analyses are "as treated") but in so doing admit possible selection bias owing to censoring.[56] Nevertheless, our findings were robust to analyses in which exposure was defined using "first treatment carried forward," which is not subject to immeasurable time bias or other selection biases due to censoring, but rather likely bias findings toward the null (especially over extended follow-up periods). Finally, it should be noted that although our study provides strong evidence against initiating adolescents and young adults with depression using high-dose antidepressant therapy, it does not address whether initiating antidepressant therapy with the most commonly prescribed (modal) dose increases or decreases the risk of DSH relative to no pharmacological treatment, or, for that matter, if our findings apply to patients with other indications. While the ques-

tion "Does prescribing antidepressants increase or decrease suicide risk?" is a question of great clinical importance (and controversy), we decided against using untreated patients as the reference group to minimize the potential for confounding by indication.

Conclusions

In our study, approximately half of all patients initiating high-dose antidepressant therapy filled prescriptions written by internists or general practitioners. This statistic, coupled with the acknowledgment that treatment decisions should be made on the basis of expected benefits and harms, underscores the relevance of our findings to clinicians caring for patients in both specialty and nonspecialty settings. Considered in light of recent meta-analyses concluding that the efficacy of antidepressant therapy for youth seems to be modest,[46,47] and separate evidence that dose is generally unrelated to the therapeutic efficacy of antidepressants,[29,40-45] our findings offer clinicians an additional incentive to avoid initiating pharmacotherapy at high-therapeutic doses and to monitor all patients starting antidepressants, especially youth, for several months and regardless of history of DSH.

ARTICLE INFORMATION

Accepted for Publication: November 18, 2013.

Published Online: April 28, 2014. doi:10.1001/jamainternmed.2014.1053.

Author Contributions: Dr Miller had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Miller, Azrael, Pate, Stürmer.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Miller, Swanson, Azrael.
Critical revision of the manuscript for important intellectual content: Azrael, Pate, Stürmer.
Statistical analysis: Swanson, Azrael, Pate, Stürmer.
Obtained funding: Miller.
Administrative, technical, or material support: Miller, Pate.
Study supervision: Miller, Stürmer.

Conflict of Interest Disclosures: Dr Stürmer does not accept personal compensation of any kind from any pharmaceutical company, although he receives salary support from the Center for Pharmacoepidemiology and from unrestricted research grants from pharmaceutical companies (GlaxoSmithKline, Merck, Sanofi) to the department of epidemiology, University of North Carolina at Chapel Hill. No other disclosures are reported.

Funding/Support: Drs Miller, Azrael, Pate, and Stürmer received support for this work from an investigator-initiated research grant (R01MH085021) from the National Institute of Mental Health (principal investigator, Dr Miller). Dr Stürmer receives investigator-initiated research funding and support as principal investigator (grant R01 AG023178) from the National Institute on Aging at the National Institutes of Health. He also receives research funding as principal investigator of the UNC-DEcIDE Center from the Agency for Healthcare Research and Quality.

Role of the Sponsor: The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

REFERENCES

1. Hammad TA, Laughren T, Racoosin J. Suicidality in pediatric patients treated with antidepressant drugs. *Arch Gen Psychiatry*. 2006;63(3):332-339.

2. Stone M, Laughren T, Jones ML, et al. Risk of suicidality in clinical trials of antidepressants in adults: analysis of proprietary data submitted to US Food and Drug Administration. *BMJ*. 2009;339:b2880.

3. Psaty BM, Siscovick DS. Minimizing bias due to confounding by indication in comparative effectiveness research: the importance of restriction. *JAMA*. 2010;304(8):897-898.

4. Bosco JL, Silliman RA, Thwin SS, et al. A most stubborn bias: no adjustment method fully resolves confounding by indication in observational studies. *J Clin Epidemiol*. 2010;63(1):64-74.

5. Patten SB. Confounding by severity and indication in observational studies of antidepressant effectiveness. *Can J Clin Pharmacol*. 2008;15(2):e367-e371.

6. Didham RC, McConnell DW, Blair HJ, Reith DM. Suicide and self-harm following prescription of SSRIs and other antidepressants: confounding by indication. *Br J Clin Pharmacol*. 2005;60(5):519-525.

7. Psaty BM, Koepsell TD, Lin D, et al. Assessment and control for confounding by indication in observational studies. *J Am Geriatr Soc*. 1999;47(6):749-754.

8. Walker AM. Confounding by indication. *Epidemiology*. 1996;7(4):335-336.

9. Ray WA. Evaluating medication effects outside of clinical trials: new-user designs. *Am J Epidemiol*. 2003;158(9):915-920.

10. Brookhart MA, Stürmer T, Glynn RJ, Rassen J, Schneeweiss S. Confounding control in healthcare database research: challenges and potential approaches. *Med Care*. 2010;48(6)(suppl):S114-S120.

11. Stürmer T, Jonsson Funk M, Poole C, Brookhart MA. Nonexperimental comparative effectiveness research using linked healthcare databases. *Epidemiology*. 2011;22(3):298-301.

12. Jick H, Kaye JA, Jick SS. Antidepressants and the risk of suicidal behaviors. *JAMA*. 2004;292(3):338-343.

13. Martinez C, Assimes TL, Mines D, Dell'aniello S, Suissa S. Use of venlafaxine compared with other antidepressants and the risk of sudden cardiac death or near death: a nested case-control study. *BMJ*. 2010;340:c249.

14. Martinez C, Rietbrock S, Wise L, et al. Antidepressant treatment and the risk of fatal and non-fatal self-harm in first episode depression: nested case-control study. *BMJ*. 2005;330(7488):389.

15. Rubino A, Roskell N, Tennis P, Mines D, Weich S, Andrews E. Risk of suicide during treatment with venlafaxine, citalopram, fluoxetine, and dothiepin: retrospective cohort study. *BMJ*. 2007;334(7587):242.

16. Schneeweiss S, Patrick AR, Solomon DH, et al. Comparative safety of antidepressant agents for children and adolescents regarding suicidal acts. *Pediatrics*. 2010;125(5):876-888.

17. Schneeweiss S, Patrick AR, Solomon DH, et al. Variation in the risk of suicide attempts and completed suicides by antidepressant agent in adults: a propensity score-adjusted analysis of 9 years' data. *Arch Gen Psychiatry*. 2010;67(5):497-506.

18. Valenstein M, Kim HM, Ganoczy D, et al. Antidepressant agents and suicide death among US Department of Veterans Affairs patients in depression treatment. *J Clin Psychopharmacol*. 2012;32(3):346-353.

19. Valuck RJ, Libby AM, Sills MR, Giese AA, Allen RR. Antidepressant treatment and risk of suicide attempt by adolescents with major depressive disorder: a propensity-adjusted retrospective cohort study. *CNS Drugs*. 2004;18(15):1119-1132.

20. Baldassano CF, Truman CJ, Nierenberg A, Ghaemi SN, Sachs GS. Akathisia: a review and case report following paroxetine treatment. *Compr Psychiatry*. 1996;37(2):122-124.

21. Hansen L, Wilkinson DG. Drug induced akathisia, suicidal ideation and its treatment in the elderly. *Int J Geriatr Psychiatry*. 2001;16(2):231-233.

22. Healy D, Whitaker C. Antidepressants and suicide: risk-benefit conundrums. *J Psychiatry Neurosci*. 2003;28(5):331-337.

23. Kasantikul D. Drug-induced akathisia and suicidal tendencies in psychotic patients. *J Med Assoc Thai*. 1998;81(7):551-554.

24. Lipinski JF Jr, Mallya G, Zimmerman P, Pope HG Jr. Fluoxetine-induced akathisia: clinical and theoretical implications. *J Clin Psychiatry*. 1989;50(9):339-342.

25. Power AC, Cowen PJ. Fluoxetine and suicidal behaviour: some clinical and theoretical aspects of a controversy. *Br J Psychiatry*. 1992;161:735-741.

26. Teicher MH, Glod CA, Cole JO. Antidepressant drugs and the emergence of suicidal tendencies. *Drug Saf*. 1993;8(3):186-212.

27. Hamilton MS, Opler LA. Akathisia, suicidality, and fluoxetine. *J Clin Psychiatry*. 1992;53(11):401-406.

28. Hansen L. Fluoxetine dose-increment related akathisia in depression: implications for clinical care, recognition and management of selective serotonin reuptake inhibitor-induced akathisia. *J Psychopharmacol*. 2003;17(4):451-452.

29. Adli M, Baethge C, Heinz A, Langlitz N, Bauer M. Is dose escalation of antidepressants a rational strategy after a medium-dose treatment has failed? a systematic review. *Eur Arch Psychiatry Clin Neurosci*. 2005;255(6):387-400.

30. Benkert O, Szegedi A, Wetzel H. Minimum effective dose for antidepressants: an obligatory requirement for antidepressant drug evaluation? *Int Clin Psychopharmacol*. 1996;11(3):177-185.

31. Dipiro JT, Talbert RL, Matzke GL, Yee GC, Wells BG, Posey ML. *Pharmacotherapy: A Pathophysiologic Approach*. 5th ed. New York, NY: McGraw-Hill Medical; 2008.

32. Taylor D, Paton C, Kerwin R. *Prescribing Guidelines*. 10th ed. London, England: Informa Healthcare; 2010.

33. Parsons L. Reducing bias in a propensity score matched-pair sample using greedy matching techniques, 2001. http://www2.sas.com/proceedings/sugi26/p214-26.pdf. Accessed October 1, 2012.

34. VanderWeele TJ. Unmeasured confounding and hazard scales: sensitivity analysis for total, direct, and indirect effects. *Eur J Epidemiol*. 2013;28(2):113-117.

35. Vanderweele TJ, Arah OA. Bias formulas for sensitivity analysis of unmeasured confounding for general outcomes, treatments, and confounders. *Epidemiology*. 2011;22(1):42-52.

36. Healy D. Lines of evidence on the risks of suicide with selective serotonin reuptake inhibitors. *Psychother Psychosom*. 2003;72(2):71-79.

37. Maris RW. Suicide. *Lancet*. 2002;360(9329):319-326.

38. Nutt DJ. Death and dependence: current controversies over the selective serotonin reuptake inhibitors. *J Psychopharmacol*. 2003;17(4):355-364.

39. Rothschild AJ, Locke CA. Reexposure to fluoxetine after serious suicide attempts by three patients: the role of akathisia. *J Clin Psychiatry*. 1991;52(12):491-493.

40. Bech P, Tanghøj P, Andersen HF, Overø K. Citalopram dose-response revisited using an alternative psychometric approach to evaluate clinical effects of four fixed citalopram doses compared to placebo in patients with major depression. *Psychopharmacology (Berl)*. 2002;163(1):20-25.

41. Bollini P, Pampallona S, Tibaldi G, Kupelnick B, Munizza C. Effectiveness of antidepressants: meta-analysis of dose-effect relationships in randomised clinical trials. *Br J Psychiatry*. 1999;174:297-303.

42. Hansen RA, Moore CG, Dusetzina SB, Leinwand BI, Gartlehner G, Gaynes BN. Controlling for drug dose in systematic review and meta-analysis: a case study of the effect of antidepressant dose. *Med Decis Making*. 2009;29(1):91-103.

43. Kelly MW, Perry PJ, Holstad SG, Garvey MJ. Serum fluoxetine and norfluoxetine concentrations and antidepressant response. *Ther Drug Monit*. 1989;11(2):165-170.

44. Ruhé HG, Booij J, v Weert HC, et al. Evidence why paroxetine dose escalation is not effective in major depressive disorder: a randomized controlled trial with assessment of serotonin transporter occupancy. *Neuropsychopharmacology*. 2009;34(4):999-1010.

45. Ruhé HG, Huyser J, Swinkels JA, Schene AH. Dose escalation for insufficient response to standard-dose selective serotonin reuptake inhibitors in major depressive disorder: systematic review. *Br J Psychiatry*. 2006;189:309-316.

46. Tsapakis EM, Soldani F, Tondo L, Baldessarini RJ. Efficacy of antidepressants in juvenile depression: meta-analysis. *Br J Psychiatry*. 2008;193(1):10-17.

47. Jureidini JN, Doecke CJ, Mansfield PR, Haby MM, Menkes DB, Tonkin AL. Efficacy and safety of antidepressants for children and adolescents. *BMJ*. 2004;328(7444):879-883.

48. Weiss JJ, Gorman JM. Antidepressant adherence and suicide risk in depressed youth. *Am J Psychiatry*. 2005;162(9):1756-1757.

49. Smith EG. Association between antidepressant half-life and the risk of suicidal ideation or behavior among children and adolescents: confirmatory analysis and research implications. *J Affect Disord*. 2009;114(1-3):143-148.

50. Braitman LE, Rosenbaum PR. Rare outcomes, common treatments: analytic strategies using propensity scores. *Ann Intern Med*. 2002;137(8):693-695.

51. D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Stat Med*. 1998;17(19):2265-2281.

52. Grobbee DE, Hoes AW. Confounding and indication for treatment in evaluation of drug treatment for hypertension. *BMJ*. 1997;315(7116):1151-1154.

53. Piper JM, Ray WA, Griffin MR. Effects of Medicaid eligibility expansion on prenatal care and pregnancy outcome in Tennessee. *JAMA*. 1990;264(17):2219-2223.

54. Strom BL, Carson JL. Use of automated databases for pharmacoepidemiology research. *Epidemiol Rev*. 1990;12:87-107.

55. West SL, Savitz DA, Koch G, Strom BL, Guess HA, Hartzema A. Recall accuracy for prescription medications: self-report compared with database information. *Am J Epidemiol*. 1995;142(10):1103-1112.

56. Suissa S. Immeasurable time bias in observational studies of drug effects on mortality. *Am J Epidemiol*. 2008;168(3):329-335.